Comprehensive measurement of long-term outcomes and costs of rehabilitation in patients with stroke

Meijeren-Pont, W. van

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Winke van Meijeren-Pont

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Wilhelmina van Meijeren-Pont

Promotor
prof. dr. T.P.M. Vliet Vlieland

Co-promotoren
dr. D.M. Oosterveer
dr. S.J. Tamminga

Leden promotiecommissie
prof. dr. W.P. Achterberg
prof. dr. S. Brouwer, Universitair Medisch Centrum Groningen
prof. dr. R. Dekker, Universitair Medisch Centrum Groningen
prof. dr. J. Gussekloo

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Table of contents

Chapter 1

General Introduction

Definition and epidemiology of stroke

Stroke, or cerebrovascular accident, is an acute neurological dysfunction caused by ischemia or haemorrhage in the brain, which persists more than 24 hours or until death[1]. Ischemic stroke is caused by an interruption of the blood supply to a part of the brain, resulting in sudden loss of function (80% of stroke patients). Haemorrhagic stroke is caused by rupture of a blood vessel or an abnormal vascular structure in the brain (20% of stroke patients)[2].

In the Netherlands, in 2020 the incidence of stroke was approximately 38.300 (20.200 men and 18.100 women) and the estimated prevalence was 511.600[3], whereas 8.890 people died because of stroke[4]. The prevalence of stroke in the Netherlands is expected to increase with 45% between 2018 and 2040, due to advances in treatment and the ageing society[3].

Acute treatment after stroke

In the acute phase of stroke, patients are usually treated in the hospital[5]. After ischemic stroke acute treatment options are thrombolysis (i.e. drug treatment aiming to disperse the clot and return the blood supply to the brain) or endovascular thrombectomy (i.e. instrumental removal of the clot from the brain)[6,7]. With the introduction of thrombolysis and thrombectomy the acute treatment of ischemic stroke has markedly improved, reducing death and functional dependency[6]. Acute treatment options of intracerebral haemorrhage consist of lowering the blood pressure, pressure release with a drain or with a neurosurgical intervention such as craniotomy, and specifically for subarachnoid haemorrhage coiling or clipping[6,7]. In contrast with ischaemic stroke, functional outcomes of patients with haemorrhagic stroke did not clearly improve over the past 20 years, but the proportion of deaths did decrease[8].

Care in the post-acute and chronic phase after stroke

In 2019, the average duration of hospital stay was 6.4 days[5]. The majority of stroke survivors (60%) is discharged home and 20% of stroke survivors are discharged to inpatient rehabilitation in a rehabilitation centre or to a geriatric rehabilitation setting[9].

Multidisciplinary inpatient and/or outpatient rehabilitation in a multidisciplinary rehabilitation centre includes a combination of physical, cognitive, mental and/or speech-language treatment modalities. Treatment is provided by a multidisciplinary team, usually comprising a rehabilitation physician, nurse, physical therapist, occupational therapist, speech-language therapist, social worker and/or (clinical) psychologist[10]. Multidisciplinary rehabilitation in a multidisciplinary rehabilitation centre is delivered in accordance with national stroke rehabilitation guidelines[9,11].

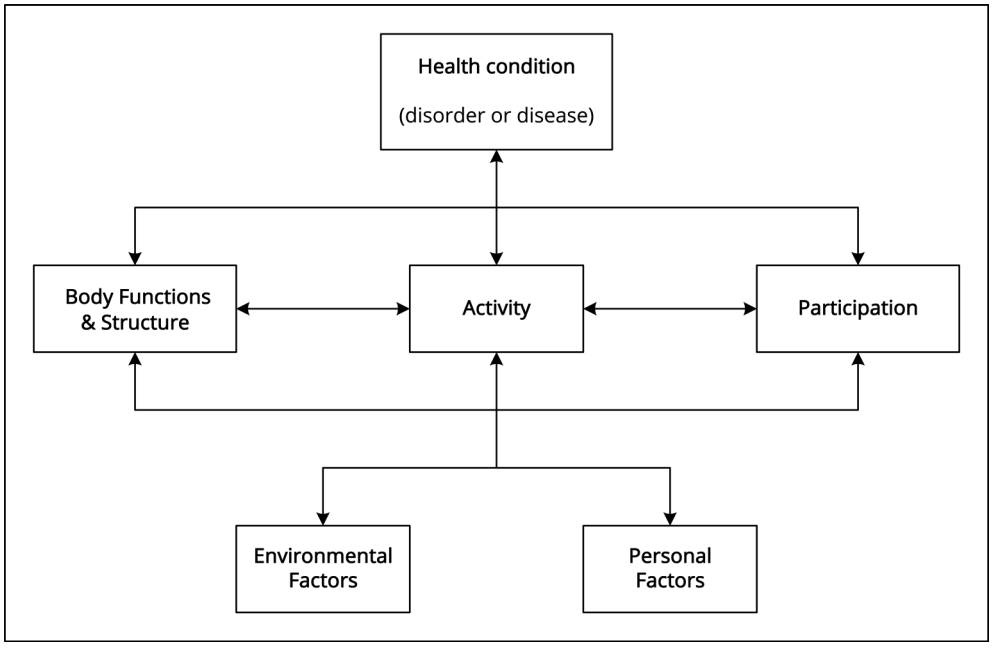
Of the patients who were discharged to their home, about two-thirds receive some form of rehabilitation treatment[12]. This may consist of either outpatient multidisciplinary rehabilitation in a multidisciplinary rehabilitation centre or primary care treatment by e.g. a speech-language therapist, physical therapist, occupational therapist or psychologist[13].

Like the situation in many countries, the costs associated with the (medical) treatment of stroke are substantial in the Netherlands and are expected to rise in the coming years[14].

Measuring outcomes after stroke

Stroke can result in physical, cognitive, emotional, communicative, social, and functional limitations[6]. In order to describe, monitor and evaluate this complexity of outcomes after stroke a comprehensive framework for health status, either or not comprising stroke-specific outcome measures, is needed. A few of these frameworks or sets of outcome measures specifically for stroke will be described in more detail.

Figure 1. The ICF Model: Interaction between ICF components.



The International Classification of Functioning, Disability and Health (ICF) Core Set for Stroke

The ICF provides a standard language to categorize health outcomes at the level of body functions and body structures, activities and participation (Figure 1)[15]. The ICF consists of two parts. Part 1, dealing with Functioning and Disability, comprises the components Body functions and body structures, and Activities and Participation. Part 2 concerns Contextual Factors, including the components Environmental Factors and Personal Factors[15]. To make the ICF more applicable for clinical practice, 'ICF Core Sets' were developed[16], comprising lists of essential categories that are relevant for specific health conditions and healthcare contexts[16]. ICF Core Sets are developed by following a scientific process based on preparatory studies and the involvement of a multidisciplinary group of experts, including health professionals and experts representing a broad range of disciplines and persons with the specific health condition[17]. In this way, the ICF Core Set for Stroke was developed, both in a comprehensive and a brief format[16]. The comprehensive ICF Core Set for Stroke contains 130 categories relevant for stroke patients[16]. The brief ICF Core Set for Stroke contains a selection of 18 of these categories, for example 'the structure of the upper extremity', 'attention function', 'walking', and 'health services, systems and policies'[16]. To facilitate the use of ICF Core Sets in clinical practice, electronic documentation forms (www.icf-core-sets.org) are available in various languages[16]. Concerning the timing of the measurements the ICF Core Sets do not provide a recommendation.

International Consortium of Health Outcome Measurement (ICHOM) Standard Set for Stroke

Building on the principles of value-based healthcare (VBHC), where the use of health outcomes data is promoted to improve outcomes important to patients and simultaneously reduce costs[18], ICHOM has developed standard sets of outcome measures for various conditions, including stroke. This ICHOM Standard Set for Stroke was developed by an international expert panel comprising stroke patients, specialties from all phases of stroke care, major international professional societies, stroke registers, and centres and was published in 2016[19]. In accordance with the three-tiered model of VBHC[18], this set comprises measures of survival and disease control, acute complications, and patient-reported outcomes and can be used in a variety of healthcare settings. Patient-reported outcomes include pain, mood, feeding, selfcare, mobility, communication, cognitive functioning, social participation, ability to return to usual activities and health-related quality of life. ICHOM recommends that baseline characteristics are recorded at admission to the hospital and that patient-reported outcome measures are recorded at discharge and at 90 days post stroke.

Minimal Data Set (MDS) Acquired Brain Injury (ABI)

ABI encompasses all types of damage to the brain that occur after birth and that are not related to progressive diseases. ABI includes, but is not limited to, stroke. A Dutch national dataset for adults with ABI was developed by 48 experts including psychologists, physicians and researchers in a three-round Delphi study and published in 2020[20]. This set of standardised measures includes the minimum amount of data necessary for obtaining a global image of the patient across all healthcare sectors (primary, secondary and tertiary care) and disciplines in every stage (i.e. acute, subacute and chronic). Twelve domains were selected, namely demographics, injury characteristics, comorbidity, cognitive functioning, emotional functioning, energy, mobility, self-care, communication, participation, social support and quality of life. These outcomes should be measured with six existing measurement instruments, two screening questions and data from a registry of demographic and injury information. The six recommended measurement instruments include the Cumulative Illness Rating Scale (CIRS), Montreal Cognitive Assessment (MoCA), Hospital Anxiety and Depression Scale (HADS), Fatigue Severity Scale (FSS), Barthel Index (BI), and Utrecht Scale for Evaluation of Rehabilitation – Participation (USER-P)[21]. The timing of the measurements is not defined.

The description of the three sets of outcomes for stroke patients makes it clear that there are a number of similarities, but also a few differences. The ICF Core Sets for stroke includes areas of functioning and contextual factors relevant for stroke patients rather than specific measurement instruments. However, electronic forms to score the presence and severity of impairments for every aspect included in the Core Sets are available[16]. The ICHOM Standard Set for Stroke does, apart from single questions, also comprise a few validated measurement instruments, in particular the Patient Reported Outcome Measurement Information System (PROMIS) Global Health (also called PROMIS-10)[19,22]. Within the MDS-ABI[21] a number of specific measurement instruments are specified, however no recommendations regarding the timing of their administration are provided. For all three abovementioned sets, clinical experience is limited with respect to their feasibility in and suitability to monitor, evaluate and improve the quality of care for stroke patients, in particular multidisciplinary rehabilitation setting.

The Stroke Cohort Outcomes of REhabilitation (SCORE) study

In 2013-2014, when the studies described in this thesis were designed, only the ICF Core Sets for stroke were available. Nevertheless, it was acknowledged at that time that, despite the availability of a few cohort studies, data on the long-term outcomes of stroke patients admitted for multidisciplinary rehabilitation were scarce. Furthermore, information on their healthcare usage and associated costs in the Netherlands were virtually absent.

For this reason, the SCORE study[10,23,24] was designed and executed in two rehabilitation centres, Rijnlands Rehabilitation Centre Leiden and Sophia Rehabilitation Den Haag (currently: Basalt) with approvement of the Medical Ethical Committee of the Leiden University Medical Centre (P13.249). The study was registered in the International Clinical Trial Registry Platform (https://trialsearch.who.int/: NTR4293). The design and execution of the study were done in close collaboration with a group of patient research partners[25], to ensure the relevance of the study for stroke patients and their caregivers.

This cohort study included all consecutive patients admitted for inpatient or outpatient multidisciplinary rehabilitation. The general aims of this study were: 1) to describe the structure and process of inpatient and outpatient stroke multidisciplinary rehabilitation, and the differences between the two centres, 2) to describe the functions, activities, participation, and quality of life of stroke patients on the short and long term, 3) to describe stroke-related costs for multidisciplinary rehabilitation, health care, and society; and 4) to determine which factors are associated with community participation of stroke patients on the long-term.

In line with these overarching aims, the study included measurements of outcomes and costs. For the selection of outcome measures the ICF served as a framework. Measurement instruments related to the ICF domains were chosen based on the literature and expert opinion. Expert opinion was derived throughout the course of the study in two ways: by means of advices and suggestions from patient research partners, a group of dedicated stroke patients (and their partners)[25], and from a steering group of scientists with background in neurology, geriatric rehabilitation, statistics, epidemiology and health economics. Based on the knowledge gaps they identified, a number of specific research questions and ensuing measurement instruments were (temporarily) added to the study protocol in the form of amendments during the conduct of the study.

The current thesis addresses six of the knowledge gaps. These gaps resulted in research questions, specifically focusing on the subgroup of stroke patients who were admitted to a multidisciplinary rehabilitation centre and, apart from the subacute (rehabilitation) phase, also on the chronic phase until 30 months after stroke. With this comprehensive description, the thesis is covering all components of the ICF, i.e. Upper extremity pain (Body functions and structures), Functional independence (Activities), Paid employment (Participation); Patient activation (Personal Factors), Caregiver Burden (Environmental factors) and Healthcare usage and costs (Environmental Factors).

Upper extremity pain

On the ICF level of Body functions and structures, pain is a common complication after stroke leading to diminished quality of life[26,27]. However, pain after stroke is often underdiagnosed and undertreated in hospital-based populations[28,29]. The upper extremity is the most common location of pain after stroke[30,31]. Nevertheless, knowledge on the development and intensity of upper extremity pain during long-term follow-up was scarce and the results of current literature were contradictory with respect to the course of upper extremity pain. A study described that the frequency of upper extremity pain increased between three and six months after stroke[31] while another study described a decrease in the frequency from four to 16 months after stroke[30].

Functional independence

In the ICF area of Activities, functional independence is an important outcome. Thus, functional independence is addressed in all outcome sets described above. Two frequently used outcome measures for functional independence are the Utrecht Scale for Evaluation of Rehabilitation (USER)[32,33] and the Barthel Index[34]. Relatively little was known on which of these outcome measures was most sensitive to change in a rehabilitation population of stroke patients and could best be used to assess functional independence.

Participation in stroke patients with paid employment

Outcomes on the Participation level are considered the most relevant and crucial outcomes of successful recovery after stroke[35,36]. Participation is a multidimensional concept comprising social participation, community participation and (return to) work[15]. Previous research found that paid work might be more important than unpaid work for stroke patients[37]. In addition, stroke patients who do not remain in paid employment reported more depressive feelings than those who are able to return to work[38,39]. These findings underline the importance of addressing both paid and unpaid employment when studying participation in stroke patients over time. However, longitudinal studies on both participation and satisfaction with participation for working patients who do or do not return to paid employment have been relatively scarce.

Patient activation

One of the internal Personal factors having an impact on a patient's health is patient activation. This is defined as one's role in the care process and having the knowledge, skills, and confidence to manage one's health and healthcare[40]. It is a prerequisite for effective self-management[41] and in the literature better patient activation was associated with better health outcomes and better care experiences in patients with chronic conditions[42]. However, in stroke patients

research on patient activation is relatively scarce, and it has not been investigated whether and to what extent it changes over time.

Caregiver burden

As an important external Environmental factor according to the ICF model, the immediate family, including the caregiver of a stroke patient has an important impact on the patient's health. Due to long lasting impairments after stroke, 49% of patients were found to receive informal care from a caregiver with an average of 76.6 hours per week one year after stroke[43]. Caregivers assist with therapy[44], they optimize recovery[45] and are important for a patient to remain active in the community[46]. However, the role of caregiver may come with a burden and result in lower quality of life[47], depression[48,49] and anxiety[47,48] for the caregiver. The individual course of caregiver burden over time was relatively unknown and might be subject to change. Therefore, it is important to know this course in order to be able to monitor caregiver burden and provide support at the right time.

Healthcare usage and costs

Next to health outcomes, costs and healthcare usage are an important part of the equation in VBHC. Despite the importance of analysing costs in VBHC, not all measurement sets for stroke mention costs and/or healthcare usage and research on costs of stroke are scarce[12]. In particular, the societal costs of stroke in the Netherlands, including costs for healthcare usage as well as for working hours lost, were understudied[12,50].

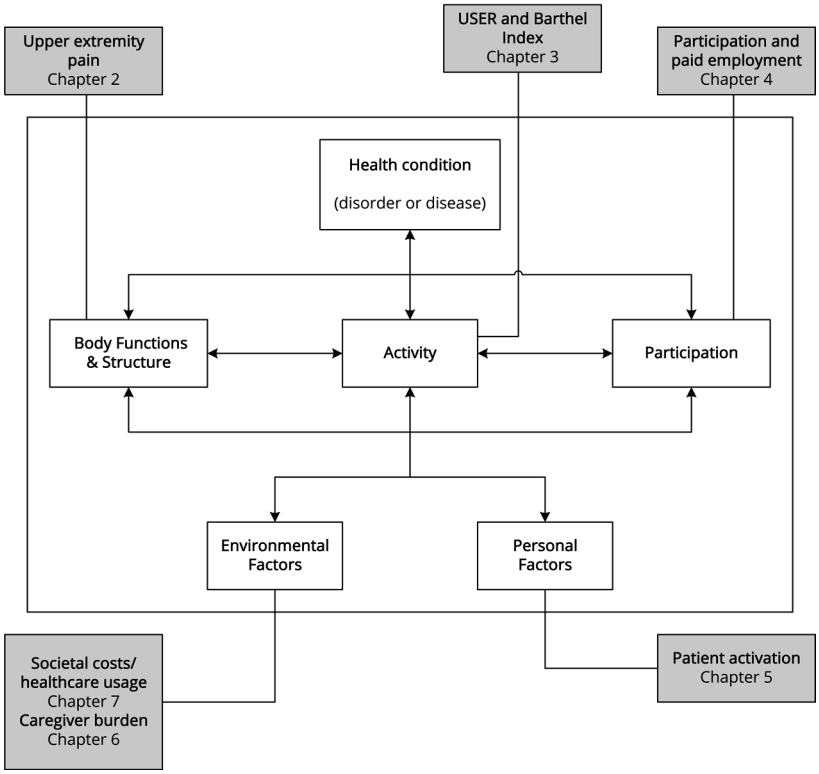
General aims and outline of this thesis

Given the abovementioned knowledge gaps, this thesis aims to comprehensively describe, in patients with stroke who were admitted in a multidisciplinary rehabilitation centre, the long-term course of pain, participation, patient activation, caregiver burden, healthcare usage and costs. Moreover, it aims to assess whether the USER or the Barthel Index can be used best to describe functional independence.

These aims are addressed in the following chapters (Figure 2):
Chapter 2 describes the course of the occurrence and severity of upper extremity pain in stroke patients at three, 18 and 30 months after the start of multidisciplinary rehabilitation.
Chapter 3 comprises a comparison of the responsiveness of the USER and the Barthel Index in stroke patients admitted for multidisciplinary rehabilitation.
Chapter 4 presents the long-term employment outcomes and participation of stroke patients who were in paid employment before stroke with comparisons of patients who do and do not return to work.

Chapter 5 describes patient activation at the start of multidisciplinary stroke rehabilitation and its course during six months follow-up.
Chapter 6 presents the course of burden for caregivers of stroke patients in the first year after the start of multidisciplinary rehabilitation.
Chapter 7 comprises an estimation of the societal costs from the start of the rehabilitation up to one year later in stroke patients who received multidisciplinary rehabilitation and an evaluation of their quality of life over time.
In *Chapter 8* the findings of the studies in this thesis are summarized and discussed.

Figure 2. Chapters of this thesis in relation to the ICF model.



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Chapter 2

The trajectory of pain and pain intensity in the upper extremity after stroke over time: a prospective study in a rehabilitation population

van Meijeren-Pont W | Arwert H | Volker G |
Fiocco M | Achterberg WP | Vliet Vlieland TPM | Oosterveer DM|
on behalf of the SCORE study group

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Abstract

Purpose

To assess the presence of upper extremity pain after stroke over time and the course of its intensity in patients with persistent pain.

Materials and methods

Patients with stroke completed a question on the presence of upper extremity pain (yes/no) and rated its intensity with a visual analogue scale (0-10) at 3, 18 and 30 months after starting multidisciplinary rehabilitation. The presence of upper extremity pain and its intensity over time were analysed with Generalized Estimating Equations models and Linear Mixed Models, respectively.

Results

678 patients were included. The proportions of patients reporting upper extremity pain were 41.8%, 36.0% and 32.7% at 3, 18 and 30 months, respectively, with the decline in proportions reaching statistical significance (odds ratio 0.82, confidence interval 0.74-0.92, $p < 0.001$). At all time points, in those reporting pain the median intensity was 5. (interquartile ranges (IQR) 4.0-7.0 at 3 and 3.0-6.0 at 18 and 30 months). In the 73 patients with persistent pain, there was no significant change in intensity over time.

Conclusions

The proportion of patients reporting upper extremity pain after stroke was considerable, despite a significant decrease in 2.5 years. In patients reporting persistent pain, the intensity did not change over time.

Introduction

Pain is a common symptom after stroke, with a prevalence of up to 50%[1,2]. The presence of pain in patients with stroke was associated with more fatigue and lower quality of life[1]. Pain after stroke was also related to anxiety, depression and even a predictor of suicidality[1-3]. However, pain after stroke remains an underrecognized medical problem[4,5]. More than one-third of patients with post-stroke pain were not treated for this pain at all[6].

The most common location of pain after stroke is the upper extremity: in 60% of patients reporting pain after stroke the upper extremity is involved, either or not in combination with pain elsewhere in their body[7,8]. Pain in the upper extremity was found to be associated with prolonged hospitalization, less functional improvement and more cognitive decline[9,10]. Risk factors associated with the development of upper extremity pain included muscle weakness, stroke severity, sensory abnormalities, spasticity and a low Barthel Index Score[10].

Knowledge on the course of upper extremity pain over time is fragmented and to some extent contradictory. Upper extremity pain is described to typically develop around three weeks after stroke[11]. Nevertheless, this pain can also develop later on as described by Hansen et al.[8] in a study with 299 patients from a hospital-based population. This study demonstrated an increase in the frequency of upper extremity pain (defined as Numeric Rating Scale ≥ 4) from 13.1% at three months to 16.4% at six months after stroke[8]. In contrast, in a population-based study with 416 patients, a much higher prevalence of upper extremity pain (defined as Visual Analogue Scale ≥ 40 mm) was reported and this prevalence decreased from 60% at four months to 45% at 16 months after stroke[7]. Besides these contradictory results, there seems to be a knowledge gap on the long-term course of pain beyond 16 months after stroke.

Therefore, the aims of the present prospective cohort study were: 1) to assess the presence of upper-extremity pain in patients with stroke until 30 months after starting rehabilitation; 2) to compare characteristics of patients with and without upper extremity pain at three months after starting rehabilitation; and, 3) to assess changes in pain intensity in patients with persistent upper extremity pain.

Materials and methods

Study design

The Stroke Cohort Outcomes of REhablitation (SCORE) study is an observational, prospective study, describing the outcomes of consecutive patients with stroke who receive multidisciplinary rehabilitation in a rehabilitation center in the Netherlands[12]. For the present study we used the collected data on pain from this sample. Rehabilitation treatment was provided by a multidisciplinary team, consisting of a rehabilitation physician, physical therapist, occupational therapist, speech therapist, social worker, psychologist and other professionals if needed. The care was delivered in either an inpatient or an outpatient setting. The intensity and duration of the multidisciplinary care depended on the capacity of the patient. Delivery of care was in accordance with the Dutch national guideline on the management of stroke[13].

The SCORE study started in March 2014 and inclusion of patients ended in December 2019. The study protocol was approved by the Medical Ethical Committee of the Leiden University Medical Center (protocol number NL465321.058.13) and is registered in the Netherlands Trial Register (number NL4293). The results are reported according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines[14].

Study sample

Consecutive patients with stroke who received inpatient or outpatient multidisciplinary rehabilitation were invited by their treating rehabilitation physician to participate in the SCORE study when they were 18 years or older and when they had a first or recurrent stroke less than six months ago. Patients with dementia or a psychiatric disorder (as reported in the referral letter from the rehabilitation physician in the referring hospital) and patients who were not able to complete questionnaires in Dutch were excluded. For inclusion in the current analyses, patients also had to have completed at least one questionnaire concerning upper extremity pain.

Procedure

In the first week of rehabilitation patients were invited by their treating physician. All patients provided written informed consent before participation.

The assessments consisted mainly of questionnaires, with the exception of clinical characteristics. Patients completed questionnaires on paper or online, depending on their preference, either or not with the help of a proxy. When there was no response within 10 days, patients were contacted by telephone or email by the study coordinator or research nurse, with a maximum of two reminders. When patients did not complete two consecutive

questionnaires they were considered lost-to-follow-up and received no further invitations to complete assessments.

The study protocol and all questionnaires were critically appraised by a panel of 8 stroke patients, the patient research partners connected to the study. Their appraisal included a review of the self-developed questions that were not part of validated questionnaires.

Measures

Sociodemographic and clinical characteristics

Age, sex and stroke type (ischemic or hemorrhagic stroke) were extracted from the patients' medical file. Alcohol usage prior to stroke, education level and living situation were collected through a questionnaire at the start of the rehabilitation (baseline). Comorbidities were assessed at baseline by the Dutch Life Situation Cohort Questionnaire, comprising 16 chronic diseases including diabetes[15].

In patients who received inpatient rehabilitation, a nurse completed the Barthel Index (BI) at baseline in the rehabilitation center and reported this in the patients' medical file. The BI measures functional dependence and ranges from 0 (i.e. totally dependent) to 20 (i.e. totally independent)[16].

Pain

At 3, 18 and 30 months after baseline patients completed questions on upper extremity pain. They were asked whether they experienced pain in their shoulder, arm, wrist or hand in the past week (hereafter called upper extremity pain). If yes, they were asked to rate the worst pain in the past week on a Visual Analogue Scale (VAS) ranging from 0 (i.e. no pain at all) to 10 (i.e. the worst imaginable pain). A VAS was previously found to be a valid and reliable method to measure pain[17]. The VAS was presented in a vertical way, to decrease the probability of bias because of visuo-spatial neglect.

Other Patient Reported Outcome Measures (PROMs)

At three months after baseline, patients completed three domains of the Stroke Impact Scale (SIS) version 3.0, the Hospital Anxiety and Depression Scale (HADS) and the EuroQol-5Dimensions-3Levels (EQ-5D-3L).

The SIS is a stroke-specific health status measure, that assesses several domains[18]. Items were rated on a five-point Likert scale and transformed to a score ranging from 0 to 100, with higher scores indicating better functioning on that specific domain. The domains Communication and Memory and thinking were administered in all patients. In April 2015, the domain Mobility was added.

The HADS consists of two subscales, measuring depressive and anxiety symptoms[19]. Each subscale comprises seven items that are rated on a four-point Likert scale, with higher scores indicating more depressive or anxiety symptoms.

The EQ-5D-3L was used to measure health-related quality of life (HR-QoL)[20]. The EQ-5D-3L consists of five dimensions (i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension has three levels of severity. The score index ranges from -0.33 (serious problems on all five dimensions) to 1 (perfect health). In addition, the EQ-5D-3L comprises a vertical VAS, ranging from 0 to 100, that is used as a quantitative measure of overall health status.

Statistical analyses

All data were anonymized when entered in a database and were analyzed with SPSS for Windows, version 25.0 (IBM Corp, Armonk, New York, USA). A two-sided *p* value of 0.05 was considered statistically significant.

Data are described as numbers (N) with percentages (%), as means with standard deviations (SD) or as medians with interquartile ranges (IQR) depending on their nature and their distribution. The Kolmogorov-Smirnov test was used to assess whether or not continuous variables were normally distributed.

Age and sex were compared between patients who did and did not complete the questions concerning pain using the Fisher's exact test or the Mann-Whitney U test. These tests were also used to compare the sociodemographic and clinical characteristics and other PROMs between patients who did and did not have upper extremity pain at three months. Patients were classified in the pain group if they had answered yes to the question whether they experienced pain in their shoulder, arm, wrist or hand in the past week and no pain if they had answered no to this question.

To assess whether the proportions of patients reporting upper extremity pain changes over time, a Generalized Estimating Equations (GEE) model with an exchangeable correlation structure was estimated with upper extremity pain (yes/no) as a dependent variable, time as independent variable, and patient as repeated subject. A GEE model was used due to the presence of repeated measurements. In order to adjust for potential confounders and interaction effects, first each characteristic or PROM was added as variable individually to the model with an interaction term with time. For each characteristic and PROM the influence on the odds ratio (OR) of having upper extremity pain over time was assessed and whether or not the interaction term was statistically significant. Secondly, each influencing variable and each significant interaction term were included in a multivariable GEE model.

To study whether or not the pain intensity measured with the VAS changed over time, a Linear Mixed Model was estimated. Time was included as independent variable and patient as random intercept in the model. This analysis was performed by using data of patients that had upper extremity pain at all time points. This was done to avoid spurious results: for patients reporting no pain at one specific time point with pain at all other time points, a VAS would be imputed as this VAS was not known leading to a relatively high estimation, while the real VAS would be low at that time point.

Results

Patients

Between March 2014 and December 2019, 836 patients with stroke were included in the SCORE study. Of these patients, 158 (18.9%) were excluded from the current analyses, because they did not complete any questionnaires on upper extremity pain. Age and sex of these excluded patients did not statistically significantly differ from those of the 678 included patients (62.0 (IQR 52.6-69.8) years versus 63.5 (IQR 55.2-70.0), p = 0.237, and 40.5% females versus 38.1% females, *p* = 0.587).

Upper extremity pain at three months

At three months after baseline, 622/678 patients completed the upper extremity pain question, with 260 (41.8%) reporting the presence of upper extremity pain.

Table 1 shows the sociodemographic and clinical characteristics and other outcome measures of patients with and without upper extremity pain at three months. Patients reporting upper extremity pain were statistically significantly more often female, more often lived alone, had more comorbidities, and had worse scores on the BI, the SIS Memory and thinking, the SIS Mobility, the HADS depression score and anxiety score and the EQ-5D-3L index and the EQ-5D-3L VAS than patients without upper extremity pain.

Table 1. Sociodemographic and clinical characteristics of patients with stroke and a comparison of those with and without upper extremity pain three months after start of rehabilitation

	All patients n = 678		**Patients *with* upper extremity pain** n = 260[2]		**Patients *without* upper extremity pain** n = 362[2]		***p* value**[3]
	n		n		n		
Age in years	617	63.7 (55.2-70.0)	258	62.9 (53.4-69.3)	359	64.3 (56.5-70.5)	0.064
Female sex	622	235 (27.8%)	260	111 (42.7%)	362	124 (34.3%)	**0.036**
Inpatient rehabilitation	622	491 (78.9%)	260	214 (82.3%)	362	277 (76.5%)	0.090
Low education level	598	221 (37.0%)	246	81 (32.9%)	352	140 (39.8%)	0.102
Living alone	599	152 (25.4%)	247	74 (30.0%)	352	78 (22.2%)	**0.036**
Alcohol use >2 a day	590	58 (9.8%)	242	22 (9.1%)	348	36 (10.3%)	0.674
Comorbidities	474	1.0 (1.0-2.0)	198	2.0 (1.0-3.0)	276	1.0 (1.0-2.0)	**0.049**
Diabetes Mellitus	599	103 (17.2%)	247	49 (19.8%)	352	54 (15.3%)	0.155
Ischemic stroke	617	499 (80.9%)	257	204 (79.4%)	360	295 (81.9%)	0.468
Barthel Index[1]	378	17.0 (11.0-19.0)	171	15.0 (10.0-19.0)	207	18.0 (13.0-19.0)	**<0.001**
SIS Communication	610	92.9 (82.1-100.0)	255	92.9 (78.6-100.0)	355	92.9 (82.1-100.0)	0.137
SIS Memory and thinking	613	89.3 (75.0-96.4)	256	85.7 (71.4-96.4)	357	89.3 (75.0-96.4)	**0.019**
SIS Mobility	376	91.7 (77.8-100.0)	157	86.1 (63.9-97.2)	219	94.4 (86.1-100.0)	**<0.001**
HADS depression score	605	4.0 (2.0-8.0)	254	5.0 (2.8-9.0)	351	4.0 (2.0-7.0)	**<0.001**
HADS anxiety score	605	4.0 (2.0-7.0)	254	5.0 (3.0-8.0)	351	4.0 (2.0-6.0)	**<0.001**
EQ-5D-3L index	604	0.81 (0.69-0.90)	249	0.73 (0.56-0.81)	355	0.86 (0.77-1.0)	**<0.001**
EQ-5D-3L VAS	607	70.0 (60.0-80.0)	251	65.0 (50.0-75.0)	356	74.0 (65.0-83.8)	**<0.001**

[1]for inpatients only [2]622/678 patients completed the pain questions at three months of whom 260 reporting and 362 not reporting upper extremity pain [3]*p* values are shown based on the Fisher exact or Mann Whitney U Test.
Abbreviations: EQ-5D-3L EuroQol-5Dimension-3Level; HADS Hospital Anxiety and Depression Scale; PROM Patient Reported Outcome Measure; SIS Stroke Impact Scale; VAS Visual Analogue Scale.
Data are described as numbers (n) with percentages (%) or as medians with interquartile ranges.

The prevalence of upper extremity pain over time

At 18 months after baseline, 519 patients completed the questions about upper extremity pain and 187 of them (36.0%) reported that they experienced upper extremity pain. At 30 months, 446 patients completed the questions and 146 (32.7%) reported that they experienced upper extremity pain. The decrease in proportions of patients reporting upper extremity pain was statistically significant (OR 0.82, confidence interval (CI) 0.74-0.92, $p < 0.001$) (Table 2).

The GEE analysis showed that sex, education level, living situation, number of comorbidities, type of stroke, BI, SIS Communication, SIS Memory and thinking, SIS Mobility, HADS depression

score and anxiety score, and EQ-5D-3L index and EQ-5D-3L VAS was associated with the outcome, and therefore these variables and PROMs were included in the multivariable model. There were no significant modifiers, therefore none of the interactions terms were added to the multivariable model. After adjusting for these characteristics and PROMs, the decrease in proportions of patients reporting upper extremity pain over time remained statistically significant (adjusted OR 0.62, CI 0.49-0.79, $p < 0.001$).

Table 2. The prevalence of pain in the upper extremity and its intensity over time in patients with stroke

	3 months		18 months		30 months		OR (CI)	*p* value
	n		n		n			
Patients reporting upper extremity pain	622	260 (41.8%)	519	187 (36.0%)	446	146 (32.7%)	0.82 (0.74-0.92)[2]	**<0.001**[2]
							0.62 (0.49-0.79)[3]	**<0.001**[3]
							β (CI)	***p* value**
Intensity of pain in all patients reporting pain at a time point[1]	259	5.0 (4.0-7.0)	187	5.0 (3.0-6.0)	146	5.0 (3.0-6.0)	*	*
Intensity of pain in 73 patients with upper extremity pain at all time points[1]	72	6.0 (5.0-7.0)	70	5.0 (4.0-7.0)	73	5.0 (4.0-7.0)	-0.22 (-0.46-0.01)	0.06[4]

[1]measured with a visual analogue scale (range 0-10) [2]OR and *p* value shown of GEE model [3]OR and *p* value shown of GEE model adjusted for confounders [4]*p* value shown of Linear Mixed model
Abbreviations: CI confidence interval; OR Odds Ratio.
Data are described as numbers (n) with percentages (%) or as medians with interquartile ranges.
*No p value calculated to avoid spurious results: for patients reporting no pain at one specific time point with pain at all other time points, a VAS would be imputed as this VAS was not known leading to a relatively high estimation, while the real VAS would be low at that time point.

Pain intensity in patients with upper extremity pain

In patients reporting upper extremity pain, the median pain intensity was 5.0 (IQR 4.0-7.0) at 3 months, 5.0 (IQR 3.0-6.0) at 18 months and 5.0 (IQR 3.0-6.0) at 30 months. There were 73 patients who reported upper extremity pain at all time points. Of these 73 patients, 69 (95%) scored the intensity of this pain on a VAS: at three months after baseline the median VAS score was 6.0 (IQR 5.0-7.0), at 18 and 30 months 5.0 (IQR 4.0-7.0). Linear Mixed Model showed that there was no significant change in pain intensity over time: β -0.22, 95% CI -0.46 – 0.01, $p = 0.06$.

Discussion

This study showed that in this sample from a rehabilitation-based stroke population taking part in an observational cohort study, the frequency of upper extremity pain statistically significantly decreased between 3 and 30 months after starting rehabilitation. Nevertheless, still 32.7% of patients reported upper extremity pain at 30 months. Patients who reported upper extremity pain at 3 months were more often female, lived alone more often, reported more comorbidities, worse functional independence, memory and thinking, mobility and

health related quality of life and a higher score for depression and anxiety than patients without upper extremity pain. In patients with persistent upper extremity pain at all time points, the intensity of pain did not diminish significantly. These results confirmed that upper extremity pain is a common problem after stroke[8] and showed that this is also the case long-term after stroke in one-third of the patients.

Characteristics of patients with stroke with upper extremity pain

In the present study, having upper extremity pain at three months after starting rehabilitation was associated with more functional dependency measured with the BI and more depressive symptoms. These associations were also found in previous studies[2,9,10]. In addition, our results showed that patients with upper extremity pain experienced more restrictions on the SIS domains Memory and thinking and Mobility. A recent study found that worse arm function measured with the Fugl–Meyer Assessment (FMA), Action Research Arm Test (ARAT), and Motor Activity Log (MAL) was associated with post-stroke complex regional pain syndrome (CRPS)[21]. Previous studies showed that pain in general after stroke was associated with female sex and with quality of life[1,4,8,9]. This study showed that these associations are also found for upper extremity pain after stroke. These results confirm that the more severely affected patients have a higher chance of experiencing upper extremity pain and that this pain seems to negatively influence quality of life.

The prevalence of upper extremity pain over time

Regarding the course of upper extremity pain in patients with stroke over time, the present study found a decrease in the presence of upper extremity pain over time. This is in accordance with results from a hospital based study on the prevalence and intensity of pain after stroke where 32% of the patients reported moderate to severe pain 4 months after stroke and 21% at 16 months[7]. The present study also found a decrease 18 months after starting rehabilitation. However, before the first measurement moment 3 months after starting rehabilitation in the present study, the frequency of pain might have increased as suggested by previous literature. Dromerick et al.[11] described that 37% of stroke patients reported hemiplegic shoulder pain on average 19 days after stroke during inpatient stroke rehabilitation. Furthermore, a more recent study in acute and follow-up stroke services also described that within 72 hours after stroke 35% of patients reported hemiplegic shoulder pain and this increased to 44% at 8-10 week follow-up[22]. These results suggest that pain arises in the subacute phase after stroke and can decrease in the chronic phase.

Despite the diminishing frequency over time, the proportion of patients experiencing upper extremity pain at all time points is still considerably higher compared to the general population. The frequency of upper extremity pain in the general population was estimated at 20.8% in a

Swedish study[23]. This higher frequency can be explained by pathophysiological mechanisms specific for stroke, such as spasticity, thalamic pain and glenohumeral joint subluxation[24].

Pain intensity in patients with upper extremity pain

Next to the relatively high frequency of upper extremity pain on the long-term after stroke, our results showed that the intensity of pain did diminish over time, but this was not statistically significant in a small subgroup of patients who reported persistent upper extremity pain. The p-value was 0.06 which might suggest that in a larger number of patients a significant decrease in pain intensity would be seen. The median VAS level of 5.0 found in these patients is in line with previous literature: Hansen et al.[8] also reported a median pain intensity level of 5 three months after stroke and Paoluccci et al.[5] reported median pain intensity levels between 5 and 6 at a follow-up duration of six months after stroke. This indicates that when pain is present the intensity is moderate to severe[7,25].

Clinical implications

These results seems to indicate that that upper extremity pain is treated suboptimal in line with the findings of Widar et al.[6]. Therefore, these results highlight the importance for clinicians to recognize upper extremity pain as a complication after stroke on the long-term, and initiate adequate treatment accordingly. Prediction models for hemiplegic shoulder pain during inpatient stroke rehabilitation as for example by Feng et al.[26] might help clinicians to identify those at risk and monitor these patients more carefully. A recent review of Dyer at al.[27] reported significant pain reduction by a wide range of treatments including orthoses, botulinum toxin injection and electrical stimulation that appear promising, however many of the included studies showed methodological limitations. This review concluded that due to the complex etiology, clinicians should consider a range of potential treatments for upper extremity pain and tailor their approach to individual presentation[22]. Furthermore, two recent reviews showed that adding botulinum toxin type A injection, pulsed radiofrequency treatment, suprascapular nerve block, intraarticular injections of novel anti-inflammatory agents, robotics, electric stimulation and trigger-point dry needling to conventional rehabilitation was significantly more effective than conventional rehabilitation alone in the treatment of patients with hemiplegic shoulder pain[28,29].

Strengths and limitations

A strength of this study is that in a large number of patients upper extremity pain was prospectively mapped with a long-term follow-up after starting stroke rehabilitation. This allowed to gain insight in the course of the frequency of upper extremity pain. In addition, we corrected for a large number of factors of influence. Another strength was that we also had data on the intensity of pain.

A limitation of this study was that the pain questionnaire did not specifically ask whether pain in the upper extremity was located on the affected side and whether this pain started after stroke. Therefore, the reported pain could be present on the affected side due to stroke, present on the unaffected side due to overuse since their stroke, or pre-existing or non-stroke related pain. Another limitation of this study is that there were no data available on whether the pain reported by the patients of our population was recognized or not, whether spasticity was involved or not, whether treatment for pain was initiated, what this treatment consisted of and whether treatment was successful or not. Thus, future research should include the nature and effect of treatment of upper extremity pain during and after rehabilitation. Finally, although patients who were considered unable to complete questionnaires in Dutch were not eligible for the present study, it can indeed not be totally ruled out that the presence of mild cognitive impairments, aphasia and/or neglect could have influenced the answers on the pain questions.

Conclusion

It can be concluded that, although the percentage of patients with upper extremity pain in a rehabilitation-based stroke sample diminished over time, about a third of patients still reported upper extremity pain up to 30 months after starting rehabilitation. If upper extremity pain persisted, its intensity did not decrease over time, with a median VAS (0-10) of 5.0. The results of the present study suggest that there is room for improvement of diagnosis and treatment of upper extremity pain in stroke patients.

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Chapter 3

Comparison of the responsiveness of the Utrecht Scale for Evaluation of Rehabilitation (USER) and the Barthel Index in stroke patients

van Meijeren-Pont W | Volker G | Vliet Vlieland TPM | Goossens PH

Clinical Rehabilitation. 2019;33(10):1672-1681.

Abstract

Objective

To compare the responsiveness of the Utrecht Scale for Evaluation of Rehabilitation (USER) to the responsiveness of the Barthel Index in stroke patients in an inpatient rehabilitation facility.

Design

Observational study.

Setting

Inpatient rehabilitation facility.

Subjects

Consecutive stroke patients admitted for clinical rehabilitation.

Interventions

Not applicable.

Main measures

The USER and the Barthel Index were administered by a nurse at admission and discharge. The Effect Size and Standardized Response Mean (SRM) were calculated as measures of responsiveness.

Results

From 198 (78%) of the 254 patients who were included in the study period, both admission and discharge data were available. At admission the mean score of the USER subscale Functional independence was 43.1 (SD = 18.9) and at discharge the mean score was 59.3 (SD = 13.8). The mean score of the Barthel Index at admission was 13.3 (SD = 5.4) and at discharge 18.4 (SD = 3.3). The Effect Size of the USER subscales Mobility, Self-care, Cognitive functioning, Pain, Fatigue and Mood were 0.85, 0.77, 0.48, 0.19, 0.40 and 0.28, respectively and of the Barthel Index 0.94. The results for the SRM were in the same range.

Conclusion

In inpatient rehabilitation after stroke, the USER was less responsive than the Barthel Index.

Introduction

The absolute number of people globally affected by stroke has substantially risen over the past decades, and acute treatment is more effective[1], resulting in an overall increase of the global burden of stroke[2]. The consequences for individual patients are often substantial[3] and thus many of them are in need of rehabilitation. In the Netherlands the majority of patients is discharged home after hospitalization for stroke, and receive rehabilitation in primary care, whereas less than 10% are referred to a rehabilitation centre for medical specialist rehabilitation[4], either in an inpatient or outpatient setting.

Regarding the measurement of outcomes of rehabilitation, appropriate outcome measures are required, both reflecting problems with specific body functions as well as addressing general functioning. Administration of such measures is not only useful for individual patients, with the aim to evaluate the rehabilitation process against set goals[5], but also from the perspective of benchmarking and monitoring the quality of care[6] on the group level.

There are many general outcome measures for stroke patients available, of which the Barthel Index[7] and the Utrecht Scale for Evaluation of Rehabilitation (USER)[8] are two examples. Particularly those two measures were included in the basic set of performance indicators that were accepted as measures of effect of clinical rehabilitation in the Netherlands since 2013[9]. The USER was found to have a good correlation with the Barthel Index and Functional Independence Measure in patients with different diagnoses, including stroke, spinal cord injury, amputation, chronic pain, multiple sclerosis, multiple trauma and various neuromuscular diseases[10]. In addition, it was found that the correlations between the USER Functional independence score and the Barthel Index score at admission and discharge in stroke patients were good[11].

For clinical practice it is important to compare similar outcome measures to see whether one offers more advantages over another, either in terms of responsiveness[12,13] or simplicity and ease-of-use, or in some other domain.

So far, little is known as to what extent all USER subscales are sensitive to changes over time in inpatient stroke rehabilitation nor have their responsiveness been directly compared with that of the Barthel Index. Therefore, the aim of the present study was to determine the responsiveness of each subscale of the USER as compared to the Barthel Index in stroke patients in inpatient rehabilitation.

Methods

This observational study was executed in Basalt Rehabilitation Leiden, the Netherlands. Patients were eligible for the present study if they were admitted for inpatient rehabilitation after between 1 January 2014 and 31 December 2015. It concerned the retrospective analysis of data which was routinely gathered according to a clinical care pathway for stroke patients who were admitted for clinical rehabilitation. For the retrospective analysis of such data, no medical ethical consent is needed according to Dutch law. The handling of data as well as the analysis and reporting was done according to Good Research Practice guidelines[14] and General Data Protection Regulation (GDPR)[15].

Rehabilitation treatment was conducted by a multidisciplinary team, consisting of a rehabilitation specialist, nurse, physical therapist, occupational therapist, speech therapist, social worker, psychologist and other professionals if needed. Treatment goals were set in cooperation with the patients, based on a comprehensive clinical assessment. Every 4 weeks multidisciplinary team conferences were held to evaluate the achievement of treatment goals. At discharge, the clinical assessment was repeated.

Criteria for admission to the rehabilitation centre, as judged by a rehabilitation physician, included recent stroke preventing the patient from living independently at home, being able to take part in at least two therapy sessions of 30 minutes each per day, having some learning ability and expecting to live independently, whether or not with spouse or caregiver, for a life expectancy of at least 1 year. Additional exclusion criteria are a diagnosis of dementia and (neuro)psychiatric conditions interfering with admittance in an open setting.

Clinical and stroke characteristics such as age, sex, stroke localization (left, right or other) and stroke type (ischemic or haemorrhagic) as well as length of stay were extracted from the medical records.

In all patients, the USER was administered by a nurse. It is a measure of functional independence that covers physical functioning (Mobility and Self-care), Cognitive functioning and additional domains of Pain, Fatigue and Mood. The USER has 30 items in total divided over six domains of which three are nurse-reported, and three patient-reported and nurse-recorded. Supplemental Appendix 1 shows the items in each subscale. The nurse-reported domains include Mobility (0-35), Self-care (0-35) and Cognitive functioning (0-50) and the nurse-recorded domains include Pain, Fatigue and Mood. Higher scores on the nurse-reported domains reflect better performance. The scores of the subscales Mobility and Self-care, are aggregated, and defined as Functional independence (0-70)[8]. An improvement of 3 points of the Functional independence scale is considered a small improvement, 7 points a moderate improvement and 14 points a large improvement[9]. For the patient-reported and nurse-recorded subscales

Pain and Fatigue, the scores range from 0 to100. The subdomains Dreariness, Grief, Fear and Anger all with a range from 0 to 100 were summed-up and defined the Mood scale (0-400). Higher scores on the Pain, Fatigue and Mood scales reflect more subjective complaints. The mean time to administer the USER was 10 minutes[8]. The inter-rater reliability of USER was found to be satisfactory to good in patients with diagnoses stroke, chronic pain, spinal cord injury, amputation and other[8].

In addition, the Barthel Index was recorded. The Barthel Index is a fully nurse-reported, 10-item measurement instrument that scores independence in activities of daily living and yields a score between 1 and 20. Higher scores indicate more independency in activities of daily living. The Barthel Index requires no direct testing and should take only minutes to administer[7]. The reported inter-rater reliability in stroke patients ranges from good to very good[16,17].

The USER and Barthel Index were collected by a nurse at admission and discharge of the patient. At the end of the rehabilitation period the USER was repeated, except if the patient was discharged from the rehabilitation facility within 6 weeks. All nurses received training each year to administer the USER. The USER and Barthel Index scores were stored in the patients' electronic medical records. Since the USER and Barthel Index were included in the basic set of performance indicators and a part of daily practice, about 30 nurses were involved in administering the USER and Barthel Index.

If the USER was administered at both admission and discharge, the patient was included in the present analysis. Furthermore, if for a subscale paired measurements were present, the patient was included in the analysis for the concerning subscale. If not, the patient was excluded from the analysis for the concerning subscale. In case of missing items no imputation was executed.

Data analyses were performed in IBM SPSS version 22 v02 (IBM Corp, Armonk, NY, 2013). Descriptive analyses were used for the patient characteristics at admission. Patient characteristics were presented as percentages, means and standard deviations for normally distributed values or medians with 25-75 percentiles (interquartile range (IQR)) and minimum and maximum for non-normally distributed variables.

Characteristics of eligible patients who were admitted in the study period, but not included in the present analysis, were compared with characteristics of patients included in the study by means of the Fisher's exact test, the independent sample's t-test and the Mann-Whitney U-test.

The difference between admission and discharge was examined by means of the paired samples t-test, as the data were normally distributed. The mean change, with the 95%

confidence interval (CI) between admission and discharge, was calculated for all USER subscales and the Barthel Index. The same was calculated without the patients with the lowest or highest possible scores. The lowest score was defined as 0 and the highest score as the highest possible score on a scale.

The responsiveness is the ability of a questionnaire to detect clinically important changes over time[13]. For each subscale of the USER the responsiveness was determined using two methods, the Standardized Response Mean (SRM) and the Effect Size. The mean change divided by the standard deviation for the mean change was used to calculate the SRM for each subscale. The Effect Size for each subscale was calculated using Cohen's *d*. The following formula was used to calculate the Effect Size (Cohen's *d*): $d = (M_0 - M_1)/SD$ in which M_0 and M_1 are the means of the baseline and follow-up measurements and *SD* is the standard deviation of the baseline measurement[18]. Cohen's *d* under 0.20 is considered a trivial effect, between 0.20 and 0.49 a small effect, between 0.50 and 0.79 a moderate effect and above 0.80 a large effect[18]. The SRM and Effect Size were calculated for all patients included in the analyses and for a subgroup without patients who had the highest or lowest possible scores. The responsiveness of the USER was compared to the responsiveness of the Barthel Index.

Floor or ceiling effects were considered to be present if more than 15% of the respondents has the lowest or highest possible score[19]. If floor and ceiling effects are present, the reliability is reduced, because patients with the lowest or highest possible score cannot be distinguished from each other. Furthermore, the responsiveness is limited, because changes cannot be measured in these patients[19]. The floor and ceiling effects were determined at admission by calculating frequency distributions.

The correlation between the USER subscale Functional independence and Barthel Index was determined using linear regression analysis.

The proportions of patients who improved, remained the same or deteriorated between admission and discharge were calculated and presented as percentages. Improvement on the subscales Mobility, Self-care, Cognitive functioning, the combined Functional independence scale and the Barthel Index was defined as a higher score at discharge than admission and deterioration as a higher score at admission than discharge. On the subscales Pain, Fatigue and Mood, improvement was defined as a lower score at discharge than admission and deterioration as a higher score at discharge than admission. A patient had a stable score when the scores at admission and discharge were exactly the same. The same was calculated without the patients with the lowest and highest possible scores.

In all statistical analyses, a p value of <0.05 was considered as statistically significant.

Results

In 2014–2015, 254 patients with a stroke were admitted for clinical rehabilitation at Basalt Rehabilitation. Figure 1 shows the flow of participants in the study. At admission, the USER scores of 240 (94.5%) patients were available. Data of 14 (5.5%) patients could not be retrieved from the database for unknown reasons. At discharge, the paired USER scores of 198 (78.0%) patients were available.

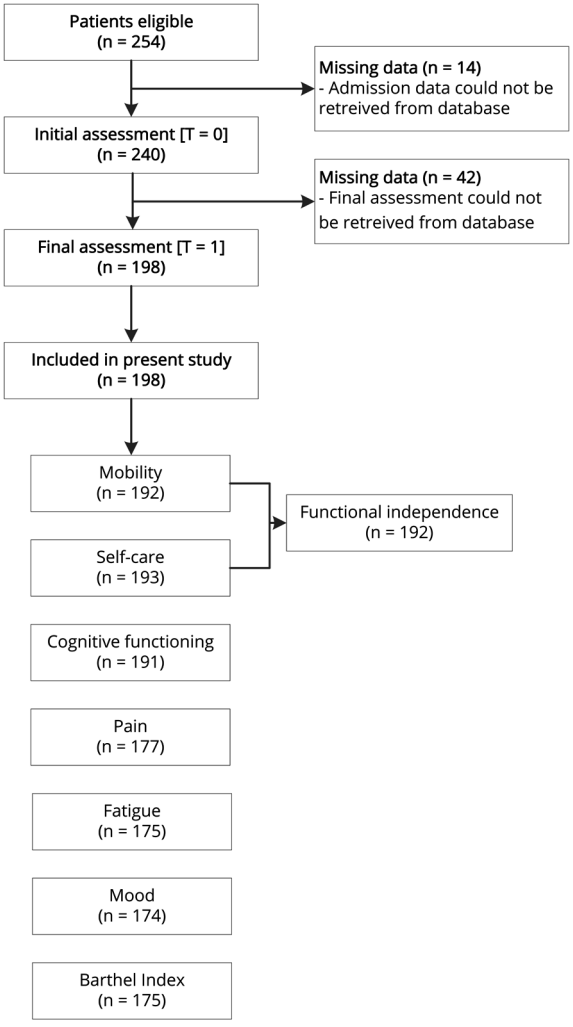


Figure 1. Flow chart of stroke patients admitted for clinical rehabilitation in one rehabilitation centre in 2014-2015 and of paired measurements for each subscale of the Utrecht Scale for Evaluation of Rehabilitation and Barthel Index.

Table 1 presents the characteristics of patients who were and who were not included in the study. There was no significant difference between the patients who were and who were not included in the study in age, percentage of males, localization of stroke, the time between stroke and admission or USER and Barthel Index scores at admission (*P*-values not shown). However, patients who were included in the present study had a significantly longer length of stay than patients who were not included in the study (*p* value 0.005).

Table 1. Characteristics of stroke patients admitted for clinical rehabilitation in one rehabilitation centre between 2014 and 2015 included and not included in the study.

	Stroke patients included in the study n = 198	**Stroke patients not included in the study** n = 42
Age, years (mean, SD)	61.5 (11.8)	58.9 (14.0)
Male (n, %)	125 (63%)	25 (60%)
Stroke localization		
Left (n, %)	91 (46%)	14 (41%)
Right (n, %)	67 (34%)	13 (31%)
Other (n, %)	26 (13%)	9 (21%)
Unknown (n, %)	14 (7%)	3 (7%)
Stroke type, ischemic (n, %)	135 (68%)	
Barthel Index (mean, SD)	13.6 (5.4) n = 192	14.0 (5.8)
Time between stroke and admission, days (median, (25-75 percentiles))	11 (7-20 n = 194	11.5 (7-19)
Length of stay, days (median, (25-75 percentiles))	52 (31-78)	35 (25-56)

Table 2 shows the USER and Barthel Index scores at admission and discharge and the Effect Size and SRM. The Effect Size for the USER subscale Pain was trivial; for the USER subscales Cognitive functioning, Fatigue and Mood the Effect Sizes were small and for the USER subscale Self-care moderate. The Effect Sizes of the Mobility and Functional independence scales and the Barthel Index were large. The calculation of the SRM yielded similar results, and a similar ranking.

The presence of floor and ceiling effects in each subscale at admission is also shown in Table 2.

Table 2. Admission and discharge scores of stroke patients admitted for clinical inpatient rehabilitation and numbers and percentages of stroke patients with the lowest and highest scores on the USER and Barthel Index at admission.

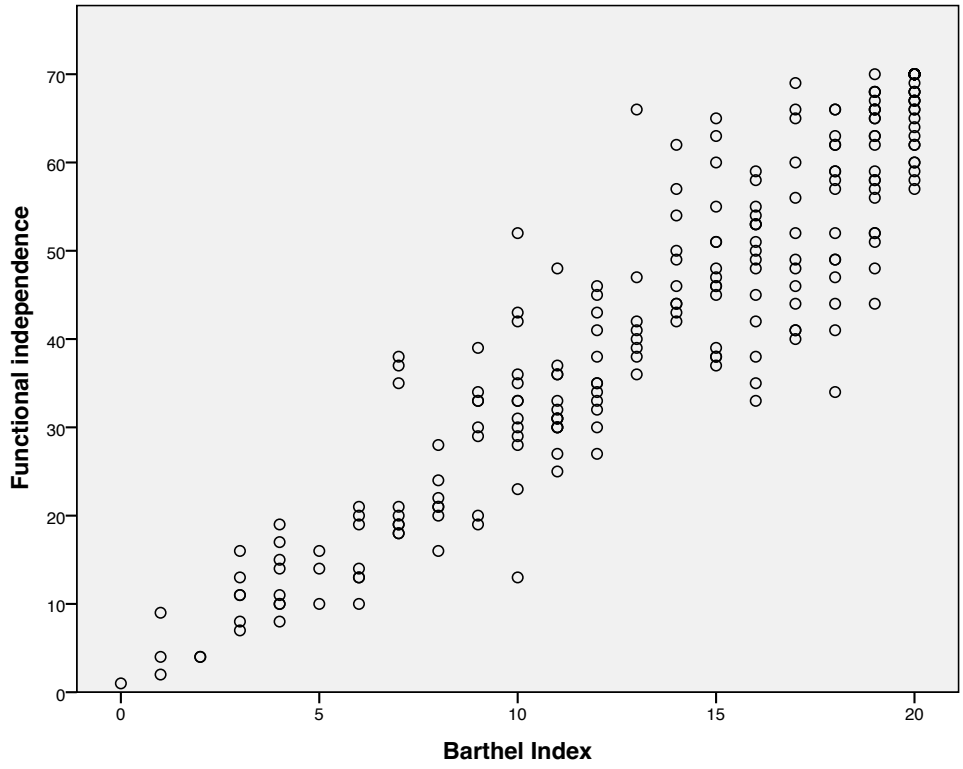
	Admission	Discharge	Mean Change (SD, CI)	SRM	ES	Lowest score (n,%)	Highest score (n,%)
All patients included in the present study							
USER Functional independence (0-70) (mean, SD) n = 192	43.1 (18.9)	59.3 (13.8)	16.3 (13.8)	1.18	0.86	1 (0.4) n = 240	21 (8.8) n = 240
Mobility (0-35) (mean, SD) n = 192	19.1 (10.5)	28.0 (8.2)	8.9 (8.2)	1.09	0.85	3 (1.3) n = 240	27 (11.3) n = 240
Self-care (0-35) (mean, SD) n = 193	23.9 (9.6)	31.3 (6.3)	7.4 (7.3)	1.01	0.77	1 (0.4) n = 240	44 (18.3)[a] n = 240
Cognitive functioning (0-50) (mean, SD) n = 191	37.5 (10.9)	42.7 (9.3)	5.1 (8.4)	0.61	0.48	1 (0.4) n = 237	29 (12.2) n = 237
Pain (0-100) (mean, SD) n = 177	17.9 (23.8)	13.4 (23.0)	-4.5 (24.5)	0.18	0.19	126 (55.0)[b] n = 229	1 (0.4) n = 237
Fatigue (0-100) (mean, SD) n = 175	40.9 (25.9)	30.5 (25.8)	-10.4 (28.5)	0.36	0.40	42 (18.4)[b] n = 228	3 (1.3) n = 228
Mood (0-400) (mean, SD) n = 174	66.7 (68.8)	47.5 (74.6)	-19.2 (79.8)	0.24	0.28	64 (28.3)[b] n = 226	0 (0.0) n = 226
Barthel Index (0-20) (mean, SD) n = 175	13.3 (5.4)	18.4 (3.3)	5.1 (4.3)	1.19	0.94	1 (0.4) n = 232	38 (16.4)[a] n = 232
Without patients with the lowest or highest scores on the subscales Self-care, Pain, Fatigue and Mood and on the Barthel index							
USER Self-care (0-35) (mean, SD) n = 160	21.6 (8.9)	30.6 (6.6)	9.0 (7.1)	1.26	1.01		
Pain (0-100) (mean, SD) n = 80	39.6 (19.7)	21.1 (28.1)	-18.5 (26.4)	0.70	0.94		
Fatigue (0-100) (mean, SD) n = 147	48.7 (20.5)	33.8 (25.1)	-14.8 (27.5)	0.54	0.73		
Mood (0-400) (mean, SD) n = 130	89.3 (65.7)	57.7 (79.5)	-31.6 (84.7)	0.37	0.48		
Barthel Index (0-20) (mean, SD) n = 149	12.2 (5.0)	18.1 (3.5)	6.0 (4.1)	1.47	1.18		

USER: Utrecht Scale for Evaluation of Rehabilitation; CI: Confidence Interval; SRM: Standardized Response Mean; ES: Effect Size; SD: Standard Deviation.
[a]Ceiling effect presents.
[b]Floor effect presents.

Table 2 also shows the Effect Size and SRM calculated without the patients who had the lowest or highest scores. The Effect Size of the Barthel Index remained large and of the USER subscale Mood remained small. The Effect Sizes of the USER subscales Self-care, Pain and Fatigue increased from moderate to large, trivial to large and small to moderate, respectively.

Figure 2 shows a scatterplot relating the results of the Barthel Index to the USER subscale Functional independence. R^2 equals 0.86.

Figure 2. Scatterplot comparing the Barthel Index with the USER subscale Functional independence.



USER: Utrecht Scale for Evaluation of Rehabilitation.

Table 3. Numbers and percentages of stroke patients improving, being stable or deteriorating according to the Barthel Index or Utrecht Scale for Evaluation of Rehabilitation (USER) between admission and discharge in inpatient rehabilitation.

	All patients included in the present study			Without patients with the lowest or highest possible score		
	Deterioration (n, %)	**Unchanged** (n, %)	**Improvement** (n, %)	**Deterioration** (n, %)	**Unchanged** (n, %)	**Improvement** (n, %)
USER						
Functional independence	7 (3.6) (n = 192)	15 (7.8) (n = 192)	170 (88.5) (n = 192)			
Mobility	9 (4.7) (n = 192)	23 (12.0) (n = 192)	160 (83.3) (n = 192)			
Self-care	8 (4.1) (n = 193)	34 (17.6) (n = 193)	151 (78.2) (n = 193)	7 (4.4) (n = 160)	2 (1.3) (n = 160)	151 (94.4) (n = 160)
Cognitive functioning	22 (11.5) (n = 191)	36 (18.8) (n = 191)	133 (69.6) (n = 191)			
Pain	36 (20.3) (n = 177)	76 (42.9) (n = 177)	65 (36.7) (n = 177)	12 (15.0) (n = 80)	3 (3.8) (n = 80)	65 (81.3) (n = 80)
Fatigue	37 (21.1) (n = 175)	38 (21.7) (n = 175)	100 (57.1) (n = 175)	27 (18.4) (n = 147)	20 (13.6) (n = 147)	100 (68.0) (n = 147)
Mood	38 (21.8) (n = 174)	40 (23.0) (n = 174)	96 (55.2) (n = 174)	27 (20.8) (n = 130)	7 (5.4) (n = 130)	96 (73.8) (n = 130)
Barthel Index	2 (1.1) (n = 175)	27 (15.4) (n = 175)	146 (83.4) (n = 175)	2 (1.3) (n = 149)	1 (0.7) (n = 149)	146 (98.0) (nf = 149)

USER: Utrecht Scale for Evaluation for of Rehabilitation; improvement: a higher score at discharge than admission; deterioration: a higher score at admission than discharge; unchanged: scores at admission and discharge were exactly the same.

Table 3 shows the numbers and percentages of patients who improved, remained the same or deteriorated on the subscales of the USER and on the Barthel Index. The largest proportions of patients (>70%) showing an improvement were seen for the USER subscales Mobility, Self-care, the combined Functional independence scale and the Cognitive functioning subscale. For the USER subscales Pain, Fatigue and Mood not only the proportions of patients who improved were lower than for the other subscales but also the proportions of patients who showed a deterioration were higher.

Table 3 also shows the numbers and percentages of patients who improved, remained the same or deteriorated on the subscales of the USER and on the Barthel Index without patients with the lowest or highest possible scores. Without patients with the highest or lowest possible score, the proportion of patients who remained the same decreased and the proportion of patients who improved increased. The proportion of patients who deteriorated was comparable between the two groups.

Discussion

This study embedded in daily practice found that overall the Barthel Index is more responsive than the USER between admission and discharge of inpatient rehabilitation in patients with stroke. The Barthel Index-related USER subscales Mobility, Self-care and Functional independence were the most responsive. The changes seen for the subscales Cognitive functioning, Fatigue, Mood and Pain were moderate to small. The lack of responsiveness of some USER subscales may in part be related to the observed ceiling and floor effects. When calculations of the Effect Size and SRM were repeated without patients with the lowest or highest possible score, the Effect Sizes of the USER subscales Self-care, Pain and Fatigue increased from moderate to large, trivial to large and small to moderate, respectively. This indicates that the floor and ceiling effects limit the responsiveness. However, the Effect Size of the USER subscale Mood still remained small and the Barthel Index still was more responsive than the most responsive subscale of the USER. Without patients with the lowest or highest possible scores, the proportion of patients who remained the same decreased and the proportion of patients who improved increased. This shows that the floor and ceiling effects observed in the USER subscales Self-care, Pain, Fatigue and Mood limit the responsiveness, because changes cannot be measured in these patients[19].

Our findings regarding USER scores are in line with results from a previous study in stroke patients executed in five different rehabilitation centres in the Netherlands. The average admission scores of 42.9, 39.1, 16.8, and 37.9 for Functional independence, Cognitive functioning, Pain and Fatigue in that study[10] were in the same range of the results of our patient group. The average admission score for the subscale Mood was higher (84.3) than we found in the present study (66.7). In that study no effect sizes or other measures of responsiveness were calculated and no comparison was made with another measure commonly used in inpatient rehabilitation, for example, the Barthel Index.

So far the responsiveness of the USER subscales has only been calculated in a population of patients with several diagnoses together, including stroke, chronic pain, spinal cord injury, amputation and other[8]. Similar to our results, in that study the subscales Mobility, Self-care and Functional independence showed large effects. The Cognitive functioning, Pain, Fatigue and Mood subscales showed a small effect. In an attempt to increase responsiveness the subscales Pain, Fatigue and Mood were changed in the process of developing the USER by the developers from a 0 to 3 scale to an 11-level numerical rating scale[8]. No further calculations of responsiveness have been done until the present study.

At admission, a floor effect was present for the subscale Pain, as 126 (55%) patients reported that they had no pain. For 35 patients (20%), the pain they experienced increased during the clinical rehabilitation period. In the literature, the reported prevalence of post-stroke pain

varies[20]. However, there is a general consensus that post-stroke pain is an underreported and under-detected phenomenon[21,22].

A limitation of this study is that it concerns a selection of patients, with patients included and not included in the study, having a significantly different length of stay. The 42 (16.5%) patients who were not included in the study and for whom no discharge data were available had significantly shorter length of stay in the rehabilitation centre than the patients for whom data on admission and discharge was available. For patients discharged from the rehabilitation centre within 6 weeks no final assessment of the USER was available, because nurses were initially trained to repeat the USER and Barthel Index every 6 weeks. Another reason might be that patients with missing data were physically independent, as was reported in a previous study concerning the main reason for the exclusion of patients missing USER data[10].

Our results may have been distorted by the fact that about 30 nurses were involved in gathering the USER and Barthel Index data, while the intra-rater reliability could not be determined. Although the relatively large number of nurses involved in data gathering reflects the reality of every day practice, a recommendation for future research is to involve a limited number of nurses in data gathering and determine the intra-rater reliability.

A way to test responsiveness is to relate the Smallest Detectable Change to the minimal important change[19]. The minimal important change is 'the smallest difference in score in the domain of interest which patients perceive as beneficial and would mandate, in the absence of troublesome side effects and excessive cost, a change in the patient's management'[23]. An anchor-based method, which uses an external criterion to determine an important change, is recommended to determine the minimal important change[19]. For future research, we recommend this method to determine the responsiveness.

In ordinal-based outcome measures, the distances between scores are separated by unknown quantities of the measured variable. Therefore, the unit distance between adjacent categories can vary in meaning across the scale[24]. To overcome this, Rasch analysis can be used[25]. This is based on log-odd transformation that determines the extent to which the observed responses fit the pattern formalized by the model. Emerging evidence shows that, compared with standard scores of ordinal scales, outcome measurement subjected to Rasch analysis shows a higher magnitude of meaningful changes over time[26,27]. For future research, we recommend that this measure is used in order to determine responsiveness.

The findings of our study may have implications for clinical practice. As indicated in the introduction, in the Netherlands the use of both the Barthel Index and the USER is advocated. Yet our study clearly demonstrated that the Barthel Index is more responsive to changes over time than the USER. As it is also more easy to administer than the USER in total, suggesting that

the use of only the Barthel Index to measure general functioning should be recommended. However, as apart from general functioning, specific functions such as speech or cognitive functioning may be affected by stroke; the use of additional outcome measures should be considered.

The Barthel Index was more responsive than the most responsive subscales of the USER in inpatient rehabilitation after stroke. A potential advantage of the USER over the Barthel Index is that it comprises dimensions of functioning other than physical functioning, such as Pain, Fatigue and Mood. However, exactly these dimensions were found to be relatively insensitive to changes over time, probably due to observed floor effects. Therefore, in clinical practice, it could be considered to use only the Barthel Index as a measure of independence in activities of daily living in stroke patients. In order to measure other common problems in stroke patients besides limitations in independence in activities of daily living, such as aphasia an cognitive functioning, other measures should be used.

Clinical messages

- The Barthel Index was more responsive than the most responsive subscales of the Utrecht Scale for Evaluation of Rehabilitation (USER) in inpatient rehabilitation after stroke.

- In clinical practice, it could be considered to use only the Barthel Index as a measure of the effect of clinical rehabilitation in stroke patients.

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Appendix 1. Utrecht Scale for Evaluation of Rehabilitation (USER) scales and items[10]

Domains	Scales	Items
Functional independence	Mobility	Sitting
		Standing
		Transfers
		Walking indoors
		Walking longer distances
		Climbing stairs
		Wheelchair mobility
	Self-care	Eating and drinking
		Grooming
		Bathing/showering
		Dressing/undressing
		Toileting
		Incontinence bladder
		Incontinence bowels
Cognitive functioning		Expressing
		Understanding
		Visual perception
		Orientation in place and time
		Attention and concentration
		Memory
		Task execution
		Initiative
		Behaviour control
		Social behaviour
Subjective complaints	Pain	
	Fatigue	
	Mood	Depressed mood
		Grief
		Anxiety
		Anger

Chapter 4

The long-term course of participation in stroke patients with paid employment

van Meijeren-Pont W | van Velzen JM | Volker G | Arwert HJ | Meesters JJL | de Kloet AJ | van Bennekom CAM | Vliet Vlieland TPM | Tamminga SJ | Oosterveer DM | on behalf of the SCORE-study group.

Submitted

Abstract

Background

Knowledge on long-term participation for patients with paid employment at the time of stroke is scarce.

Aims/Objectives

Describe the characteristics and the course of participation (concerning paid employment and overall participation) in patients who did and did not remain in paid employment.

Material and Methods

Patients with paid employment at the time of stroke completed questions on work up to 30 months after starting rehabilitation, and the Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P, Frequency, Restrictions and Satisfaction scales) up to 24 months. Baseline characteristics of patients with and without paid employment at 30 months were compared using Fisher's exact tests and Mann-Whitney U tests. USER-P scores over time were analysed using linear mixed models.

Results

Of the 170 included patients (median age 54.2 interquartile range 11.2 years; 40% women) 50.6% reported paid employment at 30 months. Those returning to work reported at baseline more working hours, better quality of life and communication, were more often self-employed and in an office job. The USER-P scores did not change statistically significantly over time.

Conclusions

About half of the stroke patients remained in paid employment.

Significance

Optimizing interventions for returning to work and achieving meaningful participation outside of employment seem desirable.

Introduction

Stroke is a common and serious medical condition[1] often leading to impairments in physical and emotional functioning, cognition, and communication[2-4], negatively influencing participation in society[5].

Regarding the course of participation on the longer term after stroke, the literature is scarce. Nevertheless, the relatively few available studies with a longer duration of follow-up showed that, despite improvements in particular in the first year, a considerable proportion of patients with stroke still experience restrictions in various aspects of participation on the longer term[6-9]. These restrictions in participation include the domain employment[9], since approximately a quarter of the patients is younger than 65 years at the time of stroke and thus part of the labour force[8]. A review of Treger et al.[10] demonstrated differences in the proportion of stroke patients that return to work between countries ranging from 14% in Germany to 73% in France and Portugal. Other reviews also mentioned wide ranges of return to work: 4.0-90.9% with a pooled summary estimate of 67.4% two years post stroke[9], 11% three months after rehabilitation to 85% seven years post stroke[11], or 0% 0-3 years post stroke to 100%, with an average of 44%[12,13]. These differences may not only reflect different international differences such as retirement age or social security systems, but may also be related to the inclusion of different stroke populations (population-based, hospital-based, rehabilitation-based), different definitions or assessment of employment status, and different follow-up durations.

Overall, it must be noted that most studies on the course of employment status report on one specific time point after stroke, usually not beyond one year, and do not describe the course of returning to work over time. Moreover, most of the studies did not report on aspects of participation other than return to paid employment, whereas participation in other meaningful activities is very important as well, both in patients who do and do not return to work.

Given that knowledge gap, the aim of the present study was to describe the long-term employment outcomes and overall participation in a Dutch cohort of stroke patients who received multidisciplinary rehabilitation and who had paid employment at the time of stroke. More specifically, the study aimed, in patients with paid employment at the time of stroke, a) to explore differences in characteristics of patients who did and did not return to work at 30 months; b) to describe the proportion of patients with paid employment and on partial or full-time sick leave over time as well as their use of employment adaptations and support; and c) to describe the course of participation in patients who did and did not remain in the work force.

Materials and methods

Study design

This study was part of the Stroke Cohort Outcomes of REhabilitation (SCORE) study[14], a longitudinal cohort study that was executed from March 2014 until December 2019 at Basalt, a multidisciplinary rehabilitation facility in the Netherlands.

The Medical Ethical Committee of the Leiden University Medical Center (protocol number NL465321.058.13) approved the SCORE study, that is registered at the International Clinical Trial Registry Platform (https://trialsearch.who.int/Default.aspx: NTR4293). The current study on the long-term course of participation is reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines[15].

Setting

In the Netherlands, after an average of six days of hospital admission for stroke, approximately 14% of the patients are referred to inpatient multidisciplinary rehabilitation in a rehabilitation facility, 15% are discharged to inpatient geriatric rehabilitation and 71% of the patients are discharged home[16]. Some of the patients who are discharged to their homes are referred to outpatient multidisciplinary rehabilitation in a rehabilitation facility[16]. As compared with geriatric rehabilitation, the population of stroke patients admitted to multidisciplinary rehabilitation is composed of the younger patients, who were more active before stroke and have complex impairments[8].

With respect to the Dutch legislation and social security system related to sick leave and work disability, it is compulsory for anyone that has paid employment with an employment contract to be insured under the Dutch Employee Insurance Schemes. This insurance obligates employers to continue to pay (a percentage of) the salary when an employee is fully or partly sick-listed during the first two years. In addition, during this period employers should do all they can to ensure that the sick employee returns to work as quickly as possible in a responsible way, including providing (temporary) modified work within the own company or elsewhere when necessary[17]. When the employee stays disabled and sick-listed for work for more than two years, the employee's 'ability to work' is examined. When this 'ability to work' is not present anymore, the employee receives a benefit of the Dutch government and the employer is allowed to terminate the employment contract of the employee. In case of self-employment this legislation does not apply; return to work is the patient's own responsibility, and it depends on his or her private insurance for sick leave and work disability whether or not he or she receives a benefit during sick leave and when there is no ability to work.

Patients

Consecutive stroke patients starting with inpatient or outpatient rehabilitation in the multidisciplinary rehabilitation facility were invited by their rehabilitation physician to participate in the SCORE study when they: 1) were 18 years or older; 2) had a first or recurrent stroke less than six months ago; 3) had no dementia or psychiatric disorder; and 4) were able to complete questionnaires in Dutch. Eligible patients who were willing to participate were only included after they provided written informed consent.

The current analysis concerned a subset of patients who had paid employment at the time of stroke, were aged <66 years (retirement age in the Netherlands in 2019) 30 months after start of rehabilitation (T30) and completed the questionnaire related to paid employment at T30.

Assessments

Sociodemographic and clinical characteristics

Sociodemographic and clinical characteristics were recorded at the start of rehabilitation, i.e. baseline. Age, sex and stroke type (i.e. ischemic or haemorrhagic stroke) were extracted from the patients' medical file. A questionnaire was used to assess educational level and living situation. Comorbidities were determined by the Dutch Life Situation Cohort Questionnaire, comprising 16 chronic diseases[18]. The Barthel Index was completed only for patients receiving inpatient rehabilitation. The Barthel Index is a nurse-reported measurement instrument that measures functional independence. It yields a score between 0 and 20, with higher scores indicating more independence[19].

Employment prior to stroke and at follow-up

A questionnaire about paid employment prior to stroke was completed at baseline and included the following questions: type of contract (permanent, temporary, self-employed, other), amount of working hours per week according to contract, type of occupation (office job, service job or industrial/manual job) and managerial position (yes/no).

At 6 (T6), 12 (T12), 18 (T18), 24 (T24) and 30 (T30) months after baseline, patients were asked whether they had paid employment (yes/no), defined as having an employment contract or being self-employed, regardless of being actually working or not (because of partial or full sick leave).

If patients indicated that they were in paid employment, an additional questionnaire was completed. They were asked whether they were actually working and/or were on partial or full sick leave. This questionnaire also comprised questions on the occurrence of employment adaptations (changes of tasks, working hours, function/position, work accommodations, or a change of employer) and support related to return to work (work-related support from

employer/supervisor, occupational physician, rehabilitation center or other), all over the past 6 months, in yes/no format.

Other Patient Reported Outcome Measures (PROMs)

Apart from the questionnaire concerning paid employment, the EuroQol-5 Dimensions-3 Levels (EQ-5D-3L)[20] and four domains of the Stroke Impact Scale (SIS) version 3.0[21] were completed at baseline. The Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P)[22] was completed at T6, T12 and T24.

The EQ-5D-3L was used to measure health-related quality of life[20]. It comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels of severity: no problems, some problems, and extreme problems. The patient is asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the five dimensions. The resulting index ranges from -0.33 (serious problems on all five dimensions) to 1 (perfect health)[23]. Next to this index, the EQ-5D-3L comprised a vertical visual analogue scale (VAS), ranging from 0 ('worst imaginable health state') to 100 ('best imaginable health state') to quantify the patient's self-rated health status[20].

The SIS is a stroke-specific health status measure, that assesses several domains[21]. Items are scored on a 5-point Likert scale and transformed to a score ranging from 0-100 for each domain, with higher scores indicating better functioning on that specific domain. The domains 'Communication' and 'Memory and thinking' were administered in all patients. In April 2015, the domains 'Mobility' and 'Mood and emotions' were added.

The USER-P is a measure that is based on the International Classification of Functioning, Disability and Health (ICF) and assesses objective and subjective participation[22]. It consists of 32 items divided into three scales: Frequency, Restrictions, and Satisfaction. The Frequency scale consists of four items on vocational activities ('paid work', 'unpaid work', 'education', 'household duties'), scored in hours per week ranging from 0 (not at all) to 5 (36 hours or more); and seven items on leisure and social activities, scored in frequency in the last four week ranging from 0 (not at all) to 5 (19 times or more). The Restrictions scale consists of 11 items on activities that may be restricted due to a health condition, including one item about 'paid work, unpaid work or education'. The perceived difficulty in performing the activity is rated on a four-point scale, ranging from 0 (not possible) to 3 (without difficulty). A 'not applicable' option is available for every item and can be used if the item is not relevant to the patient or if experienced restrictions are not related to the patient's health condition. The Satisfaction scale includes ten items on satisfaction with vocational, leisure and social activities and relationships. Items are rated on a scale from 0 (very dissatisfied) to 5 (very satisfied). For the items 'paid work, unpaid work or education' and 'your relationship with your partner' a 'not

applicable' option is available. The sum score of each scale is based on all applicable items and is converted to a 0–100 scale, with higher scores indicating better participation (more time spent/higher frequency, less restrictions, higher satisfaction)[22].

Statistical analysis

Data analyses were performed in IBM SPSS version 25 (IBM Corp: Armonk, NY, USA 2013). For all statistical analyses a two-sided *p* value of ≤ 0.05 was considered statistically significant. Data are presented as numbers (n) with percentages (%), as means with standard deviations (SD) or as medians and interquartile ranges (IQR) depending on their nature and their distribution. The Kolmogorov-Smirnov test was used to assess whether or not continuous variables were normally distributed.

Baseline sociodemographic, clinical and employment characteristics and PROMs of included patients were compared with those of patients who had paid employment at the time of stroke and were still <66 years old at T30, but who did not complete the questionnaire related to paid employment at T30 and were therefore excluded. For this comparison Fisher's exact tests and Mann-Whitney U tests were used. Baseline sociodemographic, clinical and employment characteristics and PROMs of patients with paid employment at T30 were compared with those of patients without paid employment at T30 using Fisher's exact tests and Mann-Whitney U tests, where appropriate.

The proportion of patients with paid employment was computed as the number of patients reporting they had paid employment at that time point divided by the number of patients completing the questionnaire on work at that time point. Only for patients with paid employment, the proportions of patients who were on sick leave, who had specific work adaptations and who received work-related support for each follow-up time point were calculated.

With respect to participation, the scores of each USER-P scale at T6, T12 and T24 were compared between patients with and without paid employment using Mann Whitney U tests. In order to make a fair comparison between patients with and without paid employment, additional analyses were done with the scores of each USER-P scale without the items concerning employment. For the Frequency scale it concerned omitting the items 'paid work' and 'education', as the latter is described as 'only training courses taken in the context of your paid work or to help you obtain paid work'. For the Restrictions and Satisfaction scales only the item 'paid work, unpaid work or education' was omitted. The minimum number of completed items for the Frequency scale for the first four items was set on two instead of three, and for the Satisfaction scale this was set on five instead of six.

In addition, to evaluate whether or not USER-P scores of each scale changed over time, linear mixed models were used. Analyses were done with both the complete USER-P scale scores and the scale scores without the items related to work as dependent variables. Paid employment was included in the model as being employed at T24 (yes/no). Time was the independent variable, and also an interaction term between time and paid employment at T24 was added to the model to analyse whether the slope of the change over time was different in patients with and without paid employment.

Results

Between March 2014 and December 2019, 836 patients were included in the SCORE study. Of these patients, 620 reported whether they had paid employment or not at the time of stroke: 348 (41.6%) patients reported they had paid employment at the time of stroke. Of these patients, 288 were younger than 66 years old at T30, of whom 170 (59%) completed the questionnaire related to paid employment at T30.

These 170 patients were included in the current analyses (Table 1). Their median age was 54.2 (IQR 11.2) years and 68 (40.0%) of them were female. The included patients did not statistically significantly differ from the 118 patients who had paid employment at the time of stroke and were still younger than 66 at T30, but who did not complete the employment questionnaire at T30 (Online resource 1).

Characteristics of patients with and without paid employment at T30

At T30, 86 patients (50.6%) reported to be in paid employment. Table 1 shows that compared to those who did not remain in the work force, patients with paid employment at T30 had statistically significantly more working hours and better EQ-5D-3L and SIS Communication scores at baseline. In addition, they were more often self-employed (versus permanent contract $p = 0.015$; versus temporary contract $p = 0.053$; versus other $p = 0.004$) and had more often an office job (versus service job $p = 0.026$; versus industrial/manual job $p = 0.013$).

Table 1. Baseline characteristics of stroke patients receiving multidisciplinary rehabilitation who had paid employment at the time of stroke.

		n 170	Included in the current analyses	n 86	With paid employment at T30	n 84	Without paid employment at T30	*p* value*
Sociodemographic characteristics								
Age *in years*		170	54.2 (11.2)	86	52.7 (9.3)	84	56.4 (13.2)	0.087
Female sex		170	68 (40.0%)	86	30 (34.9%)	84	38 (45.2%)	0.210
Low education level		167	46 (27.1%)	85	20 (23.5%)	82	26 (31.7%)	0.299
Living alone		169	30 (17.8%)	86	13 (15.1%)	83	17 (20.5%)	0.423
Clinical characteristics								
Ischemic stroke		167	126 (75.4%)	84	63 (75.0%)	83	63 (75.9%)	1.000
Number of comorbidities		131	1.0 (1.0)	64	1.0 (2.0)	67	1.0 (1.0)	0.054
Barthel Index at start rehabilitation[1]		92	17.0 (9.0)	44	17.0 (8.0)	48	17.0 (9.0)	0.803
Employment characteristics prior to stroke								
Type of contract	Permanent	170	131 (77.1%)	86	64 (74.4%)	84	67 (79.8%)	**0.008**
	Temporary		12 (7.1%)		5 (5.8%)		7 (8.3%)	
	Self-employed		20 (11.8%)		16 (18.6%)		4 (4.8%)	
	Other		7 (4.1%)		1 (1.2%)		6 (7.1%)	
Number of working hours according to contract		169	36.0 (11.0)	86	38.0 (4.0)	83	35.0 (16.0)	**0.001**
Type of occupation	Office job	155	67 (43.2%)	79	43 (54.4%)	76	24 (31.6%)	**0.014**
	Service job		51 (32.9%)		22 (27.8%)		29 (38.3%)	
	Industrial or manual job		37 (23.9%)		14 (17.7%)		23 (30.3%)	
Managerial position		154	18 (11.7%)	79	13 (16.5%)	75	5 (6.7%)	0.079
Patient Reported Outcome Measures								
EQ-5D-3L index		151	0.78 (0.26)	77	0.81 (0.21)	74	0.77 (0.34)	**0.008**
EQ-5D-3L VAS		159	65.0 (26.0)	81	70.0 (20.0)	78	60.0 (31.0)	**0.003**
SIS Communication		161	92.2 (25.0)	84	96.1 (17.9)	77	89.3 (28.6)	**0.035**
SIS Mobility		84	84.7 (38.2)	39	91.7 (36.1)	45	83.3 (52.8)	0.207
SIS Memory and thinking		163	85.7 (25.0)	84	85.7 (24.1)	79	82.1 (32.1)	0.132
SIS Mood and emotions		84	79.2 (23.6)	39	80.6 (19.4)	45	75.0 (23.6)	0.183

Dichotomous variables are described as numbers with percentages (%) and continuous variables as medians with interquartile ranges; **p* values are given of Fisher Exact Tests or Mann-Whitney U Tests, when appropriate.
[1]For inpatients only
Abbreviations: EQ-5D-3L EuroQoL-5 Dimensions-3 Levels; SIS Stroke Impact Scale; VAS visual analogue scale.

Table 2. Employment outcomes at all follow-up time point of patients who had paid employment at the time of stroke.

	n	6 months	n	12 months	n	18 months	n	24 months	n	30 months
Employment	159		158		153		154		170	
No paid employment		25 (15.7%)		25 (15.8%)		38 (24.8%)		64 (41.6%)		84 (49.4%)
Paid employment		134 (84.3%)		133 (84.2%)		115 (75.2%)		90 (58.4%)		86 (50.6%)
Presence of sick leave when employed	93		88		81		62		50	
Working without sick leave		9 (9.7%)		30 (37.5%)		43 (53.1%)		50 (80.6%)		41 (82.0%)
Partial sick leave		27 (29.0%)		35 (39.8%)		21 (25.9%)		7 (11.3%)		5 (10.0%)
Full sick leave		57 (61.3%)		23 (26.1%)		17 (21.0%)		5 (8.1%)		4 (8.0%)
Employment adaptations when employed[1]	92		133		114		90		86	
No employment adaptations		53 (57.6%)		67 (50.4%)		65 (57.0%)		57 (63.3%)		74 (86.0%)
Work tasks/activities		24 (26.1%)		32 (24.1%)		22 (19.3%)		13 (14.4%)		7 (8.1%)
Working hours		24 (26.1%)		38 (28.6%)		23 (20.2%)		9 (10.0%)		8 (9.3%)
Work function/position		3 (3.3%)		11 (8.3%)		9 (7.9%)		5 (5.6%)		5 (5.8%)
Work accommodations (e.g. devices)		5 (5.4%)		12 (9.0%)		6 (5.3%)		5 (5.6%)		1 (1.2%)
Change in employer		0 (0.0%)		3 (2.3%)		4 (3.5%)		3 (3.3%)		1 (1.2%)
Employment-related support[1]	92		133		114		90		86	
No employment-related support		34 (37.0%)		55 (41.4%)		65 (57.0%)		64 (71.1%)		80 (93.0%)
Employer/supervisor		34 (37.0%)		53 (39.8%)		29 (25.4%)		10 (11.1%)		4 (4.7%)
Occupational physician		38 (41.3%)		55 (41.4%)		36 (31.6%)		16 (17.8%)		4 (4.7%)
Rehabilitation centre		26 (28.3%)		23 (17.3%)		4 (3.5%)		3 (3.3%)		1 (1.2%)
Other		5 (5.4%)		10 (7.5%)		15 (13.2%)		4 (4.4%)		1 (1.2%)

Variables are described as numbers with percentages (%).
[1]In the previous six months in the patients who had paid employment at that specific follow-up time point; several answers were possible when patients reported that there were employment adaptations or that they received employment-related support.

Paid employment over time

Table 2 shows the employment status of the 170 participants over time. The proportions of patients reporting that they were employed decreased, in particular between T18 and T24, with eventually 50.6% of patients reporting paid employment at T30. Only few patients reported changing jobs. The individual courses of patients of employment status are described in Online Resource 2.

Patients reporting paid employment could also be on sick leave partially or fully. Although the proportions of patients in paid employment decreased over time, among those with paid employment, the percentage of patients reporting that they were working without sick leave increased from 9.7% at T6 to 82.0% at T30. It must be noted that at the various follow-up time points, only 58.1%-70.4% of patients reporting paid employment provided information on sick leave.

Employment adaptations and support

Table 2 also provides insight into the implementation of employment adaptations and the support from the employer or health professionals with respect to return to work. It appeared that overall changes in tasks and activities and changes in working hours were the most frequently reported employment adaptations. With regard to support the guidance from the employer/supervisor and occupational physician were reported more often than that from the rehabilitation center or other sources. Like the questions on sick leave, the response rates to the questions on employment adaptations and support at the various time points were varying between 68.7%-100.0%.

Participation over time

Table 3 shows the scores of all three USER-P scales of the total group of patients and separately for patients either reporting or not reporting paid employment at T6, T12 and T24.

Regarding the differences of USER-P scale scores between patients with and without paid employment, there were no statistically significant differences at T6, whereas at T12 patients reporting paid employment had significantly better scores for the USER-P Frequency and Restrictions scales ($p < 0.05$) and at T24 for all three USER-P scales (all $p < 0.001$). With respect to USER-P scale scores over time, there were no statistically significant changes over time, neither in the total, nor within the subgroups of patients with or without paid employment at T24 (Online Resource 3).

When leaving out the items concerning employment, again at T6 no statistically significant differences in USER-P scale scores were seen between patients who did and did not report paid employment at that time point. At T12 only the difference for the Restrictions scale remained. At T24, the scores for the Restrictions and Satisfaction scales were statistically significantly better for patients with paid employment, whereas the Frequency scale score was not statistically significantly different. Regarding the course of the Frequency scale score, its scores diminished over time for patients with paid employment (β -1.74, 95%CI -2.96 – -0.52, $p = 0.005$), but not in patients without paid employment at 24 months.

Table 3. USER-P in stroke patients with and without paid employment up to 24 months after the start of rehabilitation.

	n	6 months	*p* value*	n	12 months	*p* value*	n	24 months	*p* value*
USER-P Frequency									
All items									
All patients	159	33.6 (16.4)		160	33.6 (14.8)		158	31.4 (16.3)	
Paid employment	131	34.6 (17.5)	0.182	133	34.6 (15.0)	**0.001**	90	36.0 (17.0)	**<0.001**
No paid employment	25	29.2 (13.0)		25	28.9 (16.3)		61	29.3 (10.4)	
Without item 'Paid work' and 'education'									
All patients	159	34.3 (15.7)		160	33.1 (14.8)		158	32.9 (16.8)	
Paid employment	131	34.3 (16.4)	0.470	133	33.6 (14.3)	0.799	90	31.8 (17.9)	0.697
No paid employment	25	33.6 (17.3)		25	33.3 (23.6)		61	34.3 (13.6)	
USER-P Restrictions									
All items									
All patients	161	83.3 (33.0)		157	87.5 (27.3)		158	87.9 (33.3)	
Paid employment	133	83.3 (33.2)	0.197	130	89.4 (27.9)	**0.005**	90	96.8 (19.0)	**<0.001**
No paid employment	25	76.7 (43.3)		25	74.1 (35.3)		61	70.0 (30.8)	
Without item 'Paid work, unpaid work or education'									
All patients	161	86.7 (33.3)		157	90.0 (30.0)		158	90.0 (29.3)	
Paid employment	133	88.9 (33.3)	0.284	130	92.6 (26.7)	**0.032**	90	96.7 (18.5)	**<0.001**
No paid employment	25	80.0 (42.1)		25	74.1 (34.6)		61	73.3 (29.6)	
USER-P Satisfaction									
All items									
All patients	158	72.2 (27.1)		157	72.5 (25.8)		155	72.5 (27.5)	
Paid employment	130	72.2 (26.9)	0.713	130	72.5 (26.3)	0.093	90	77.6 (26.5)	**<0.001**
No paid employment	25	75.0 (33.8)		25	69.4 (29.5)		58	65.6 (27.8)	
Without item 'Paid work, unpaid work or education'									
All patients	158	75.0 (25.7)		158	75.0 (25.3)		158	75.0 (26.2)	
Paid employment	130	75.0 (25.0)	0.813	131	75.0 (26.7)	0.064	90	77.8 (26.9)	**<0.001**
No paid employment	25	75.0 (32.5)		25	69.4 (29.3)		61	69.4 (26.4)	

Variables are described as medians with interquartile ranges; **p* values are given of Mann-Whitney U Tests comparing patients with and without paid employment.
Abbreviations: USER-P Utrecht Scale for Evaluation of Rehabilitation–Participation.

Discussion

This study on the long-term course of employment outcomes and overall participation in patients with paid employment pre-stroke receiving multidisciplinary rehabilitation, found that half of them reported paid employment at 30 months after starting rehabilitation. The proportion of patients that had paid work was highest at six months with a marked decrease between 18 and 24 months after start of rehabilitation. These results reflect the Dutch social security system, where patients who are employed but sick-listed are entitled to a two-year period of (partial) salary payment and possible re-integration.

Baseline characteristics of employment, namely self-employment, a higher number of working hours and having an office job were associated with having paid employment at T30. In addition, the patients remaining in the work force reported better quality of life and less impact of their stroke on communication at baseline.

With respect to participation that is not employment related, patients who reported paid employment experienced less restrictions and were more satisfied than patients who did not. However, frequencies of participation outside of employment did not differ and decreased with time in those who retained work.

Our study showed a decrease in proportions of patients reporting paid employment that seems in contrast to previous studies such as that of Saeki et al.[24], that demonstrate an increase of patients that return to work over time. Nevertheless this contrast is not an actual contrast, because looking at the proportions of patients that reported paid employment and actually worked the same increase over time is seen.

In our study, half of the patients returned to paid employment at 30 months, but it is difficult to directly compare this result with previous studies, in part due to methodological differences. Therefore, and as mentioned in the introduction, estimated proportions of stroke patients returning to work varied largely[9-12]. Nevertheless, our finding is in the same range as the proportions seen in a previous Dutch cross-sectional, hospital-based study including patients aged 18-65 years at 2-5 years post-stroke, where 39% returned to work[25]. The patients of that study were younger and more often had an ischemic stroke than the patients in our study, but the proportions females and patients with a low level of education were comparable. In addition, our results were in the same range of a review which calculated a pooled summary estimate of return to work two years post-stroke of 67.4%[9]. Overall, the heterogeneity in study methodology seen in the studies on this topic underlines the need for international consensus on how to best define and assess employment status in clinical and epidemiological studies in stroke patients[10,26,27].

This quantitative study did not elaborate on why patients were not able to return to paid employment. Depending on the patient's health status, the work situation, and the social security system, the work status of patients may vary largely within and across patients, with possible combinations of either or not working fully or partially and either or not being on fulltime or parttime sick leave, and either or not receiving a fulltime or parttime disability pension. For a detailed description an individual interview or an extensive questionnaire is needed.

Regarding the association of baseline characteristics with long-term paid employment, our findings are in general in line with previous literature. Regarding work characteristics, previous

literature in particular demonstrated that white collar occupation was beneficial for return to work compared to blue collar occupation (24,28). Our study found that self-employment and more working hours at baseline were also associated with return to work.

Regarding stroke characteristics, previous studies found that the presence of aphasia was negatively associated with return to work[28,29], which is in line with the observation in our study that the SIS Communication score was lower in patients who did not return to work.

Moreover, it has been found previously that normal muscle strength, absence of apraxia and more independence in activities of daily life measured with the Barthel Index were positively related to return to work[24,29], while other studies showed no influence of stroke severity[30]. In our study, better scores for the EQ-5D-3L, which involves questions about mobility and activities of daily life, were associated with paid employment at T30. However this was not true for the SIS Mobility nor for the Barthel Index, perhaps because of low number of patients for whom these outcomes were known.

This study found that at all time points, a considerable proportion of patients reported employment adaptions in the previous six months, with only few changing jobs. The need for reductions in working hours and employment modifications because of changes in abilities due to stroke are previously mentioned in literature[10]. However, our results are hard to compare with those from other studies, as we did not record the cumulative, overall changes from baseline onwards. However, by recording adaptations over the previous six months, we were able to demonstrate that the occurrence of adaptations in those with paid employment decreased with time. It remains unclear to what extent this finding can be interpreted as a decreasing need and successful work integration over time.

Support from the employer and occupational physician were the most often reported sources of help. Although we have no cumulative figures, the findings at six months can be interpreted on their own, where it is striking that less than half of the patients reported support from their employer or occupational physician. These results may be flattened by the reporting of self-employed patients, but nevertheless may indicate that there is room for improvement, in particular given the far-reaching legal responsibility to support the return to work process in the Netherlands[26]. Work-directed interventions in combination with education/coaching were shown previously to be effective regarding return to work[31]. It could be considered to include these interventions more consistently by the employer, occupational physician or rehabilitation center.

Considering participation outside of paid employment, it was striking that although frequencies were comparable, patients without paid employment experience more restrictions and less satisfaction with this participation. A previous study demonstrated that stroke patients retain predominately more sedentary and home-based activities and fewer physically demanding

and community based activities[32]. This might be more the case for patients without paid employment, explaining the difference in restrictions and satisfaction. Indeed, a need for well-founded, proven effective interventions for achieving meaningful participation outside of employment has been mentioned previously[33]. It was suggested that this might require different types of support at various stages after stroke[34] and should take into account the social support system and other environmental factors, such as transportation[35,36].

Strengths and limitations

A strength of this study is the long-term, prospective design and the comprehensive assessment of both employment and participation. The computation of the USER-P scale scores with and without work-related items allowed a fair comparison on the perception of participation of patients who remained in paid employment and who did not. Limitations include the relatively small sample size, inclusion from only one rehabilitation facility and missing items in questionnaires of patients in the study. Moreover, the study population was selected based on their completion of the 30-months assessment. Although their characteristics at baseline did not differ from those who did not complete the study, selection bias cannot be ruled out. Another limitation was that the definition of ´having paid employment´ could reflect different situations, including being actually at work or being fully or partly sick-listed. Although we aimed to gather detailed information from all patients, the precise working situation was missing for a proportion of patients. Finally, the results from the present study are influenced by the Dutch context and might therefore not be applicable to other countries with different legislation, social security and health systems.

In conclusion, the results of the present study suggest that there are windows of opportunity to improve the participation outcomes for patients in paid employment at the time of stroke receiving rehabilitation, both in those who do and do not remain in the work force, by implementing more consistently effective work-directed interventions and interventions for achieving meaningful participation outside of employment.

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Online Resource 1. Baseline characteristics of stroke patients receiving multidisciplinary rehabilitation who had paid employment at the time of stroke

		n 170	Included in the current analyses	n 118	Excluded in the current analyses	*p*-value*
Sociodemographic characteristics						
Age *in years*		169	54.2 (11.2)	115	53.9 (13.2)	0.839
Female sex		170	68 (40.0%)	118	51 (43.2%)	0.627
Low education level		167	46 (27.5%)	116	43 (37.1%)	0.093
Living alone		169	30 (17.8%)	115	29 (25.2%)	0.138
Clinical characteristics						
Ischemic stroke		167	126 (75.4%)	117	90 (76.9%)	0.888
Number of comorbidities		131	1.0 (1.0)	97	1.0 (2.0)	0.832
Barthel Index at start rehabilitation[1]		92	17.0 (9.0)	70	17.0 (9.0)	0.494
Employment characteristics						
Type of contract	Permanent	170	131 (77.1%)	118	84 (71.2%)	0.668
	Temporary		12 (7.1%)		11 (9.3%)	
	Self-employed		20 (11.8%)		16 (13.6%)	
	Other		7 (4.1%)		7 (5.9%)	
Number of working hours according to contract		169	36.0 (11.0)	116	36.0 (16.0)	0.119
Type of occupation	Office job	155	67 (43.2%)	97	37 (38.1%)	0.219
	Service job		51 (32.9%)		27 (27.8%)	
	Industrial or manual job		37 (23.9%)		33 (34.0%)	
Managerial position		154	18 (11.7%)	98	11 (11.2%)	1.000
Patient Reported Outcome Measures						
EQ-5D-3L index		151	0.78 (0.26)	108	0.76 (0.35)	0.191
EQ-5D-3L VAS		159	65.0 (26.0)	108	64.0 (25.0)	0.528
SIS Communication		161	92.2 (25.0)	109	89.3 (26.8)	0.245
SIS Mobility[2]		84	84.7 (38.2)	80	86.1 (29.9)	0.492
SIS Memory and thinking		163	85.7 (25.0)	111	78.6 (35.7)	0.270
SIS Mood and emotions		84	79.2 (23.6)	82	77.8 (22.2)	0.526

Dichotomous variables are described as numbers with percentages (%) and continuous variables as medians with interquartile ranges; **p*-values are given of Fisher Exact Tests or Mann-Whitney U Tests, when appropriate.
[1]For inpatients only
[2]Added later to the set of questionnaires
Abbreviations: EQ-5D-3L EuroQoL-5 Dimensions-3 Levels; SIS Stroke Impact Scale; VAS visual analogue scale.

Online Resource 2. Overview of employment status at the different measurement moments of stroke patients with paired measurements.

	n 126	6 months	12 months	18 months	24 months	30 months
Group 1 Paid employment at all measurement moments						
	54 (42.9%)	+	+	+	+	+
Group 2 Paid employment over time						
Paid employment at 12, 18, 24 and 30 months	5 (4.0%)	-	+	+	+	+
Paid employment at 18, 24 and 30 months	0 (0.0%)	-	-	+	+	+
Paid employment at 24 and 30 months	2 (1.6%)	-	-	-	+	+
Paid employment at 30 months	0 (0.0%)	-	-	-	-	+
Group 3 No longer paid employment over time						
No longer paid employment at 12, 18, 24 and 30 months	6 (4.8%)	+	-	-	-	-
No longer paid employment at 18, 24 and 30 months	9 (7.1%)	+	+	-	-	-
No longer paid employment at 24 and 30 months	20 (15.9%)	+	+	+	-	-
No longer paid employment at 30 months	12 (9.5%)	+	+	+	+	-
Group 4 Having paid employment fluctuates over time						
Paid employment at 6, 18, 24 and 30 months	1 (0.8%)	+	-	+	+	+
Paid employment at 6, 12, 24 and 30 months	4 (3.2%)	+	+	-	+	+
Paid employment at 6, 12, 18 and 30 months	1 (0.8%)	+	+	+	-	+
Paid employment at 6 and 18 months	1 (0.8%)	+	-	+	-	-
Paid employment at 12 months	2 (1.6%)	-	+	-	-	-
Group 5 No longer paid employment after baseline						
	9 (7.1%)	-	-	-	-	-

+ means paid employment at that measurement moment
- means no paid employment at that measurement moment

Online Resource 3. Linear mixed model results of USER-P scales over time

	Complete USER-P scale			USER-P scale without items paid employment		
	β	95% CI	*p*-value	β	95% CI	*p*-value
USER-P Frequency scale						
Time	-0.62	-1.97 – 0.74	0.370	0.45	-1.03 – 1.93	0.550
Paid employment at T24	7.81	3.31 – 12.31	**0.001**	6.77	1.82 – 11.71	**0.007**
Time*Paid employment at T24	0.52	-1.23 – 2.28	0.557	-2.19	- 4.11 – -0.27	**0.026**
USER-P Restrictions scale						
Time	1.19	-0.87 – 3.26	0.257	1.41	-0.59 – 3.41	0.166
Paid employment at T24	16.54	9.28 – 23.80	**<0.001**	15.24	8.16 – 22.32	**<0.001**
Time*Paid employment at T24	0.60	-2.08 – 3.29	0.659	-0.19	-2.78 – 2.41	0.888
USER-P Satisfaction scale						
Time	0.45	-1.50 – 2.39	0.652	0.09	-1.84 – 2.02	0.930
Paid employment at T24	12.78	5.48 – 20.07	**0.001**	12.44	5.12 – 19.77	**0.001**
Time*Paid employment at T24	0.31	-2.17 – 2.80	0.804	0.10	-2.38 – 2.59	0.935

Abbreviations: CI confidence interval; T24 time measurement point 24 months after start of the rehabilitation; USER-P Utrecht Scale for Evaluation of Rehabilitation–Participation.

Chapter 5

Patient activation during the first 6 months after the start of stroke rehabilitation

van Meijeren-Pont W | Tamminga SJ | Fiocco M | Gonzalez Avila A | Volker G | Janssen SMJ | Vliet Vlieland TPM | Oosterveer DM | on behalf of the SCORE study group

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Abstract

Objective

To examine patient activation from the start of stroke rehabilitation and its course up until the 6-month follow-up.

Design

Inception cohort study with a follow-up of 6 months.

Setting

Multidisciplinary rehabilitation facility.

Participants

A total of 478 stroke patients (n=478) who received inpatient or outpatient rehabilitation, with a median age of 63.0 years (interquartile range, 56.0-70.0 years) with 308 (64.2%) being men. The study was completed by 439 (91.8%) patients.

Interventions

Not applicable.

Main Outcome Measures

Patient activation was measured with the Patient Activation Measure (PAM) (score 0-100, 4 levels, where a higher score and level denotes more patient activation). The PAM was measured at the start of the rehabilitation (baseline) and 3 and 6 months thereafter and was analyzed using the multivariate mixed model analysis.

Results

At baseline, the mean PAM score was 60.2±14.3, with the number of patients in PAM levels 1, 2, 3, and 4 being 76 (17.8%), 85 (19.9%), 177 (41.4%), and 90 (21.0%), respectively. The multivariate mixed-model analysis demonstrated that the PAM score increased over time (baseline 60.2±14.3) vs 3 months 60.7±14.8 vs 6 months 61.9±18.0; *P* .007). Between baseline and 6 months, 122 patients (41.4%) remained at the same PAM level, 105 patients (35.6%) increased, and 68 patients (23.1%) decreased. At all time points, >35% of patients were in level 1 or 2.

Conclusions

PAM scores increased slightly over time from the start of rehabilitation up to the 6 month follow-up. However, more than one-third of patients remained at low levels (ie, level 1 and 2) of patient activation, which indicates that specific interventions during rehabilitation to increase patient activation might be of value.

Introduction

Stroke is a common health problem worldwide, leading 50% of patients to develop a chronic condition with a combination of motor, communication, cognitive, or emotional limitations[1-5].

In patients with chronic conditions, such as stroke, self-management is of great importance[6]. Self-management refers to the strategies, decisions, and activities individuals take to manage a long-term health condition[7]. Specifically in patients with stroke, 3 subdomains of self-management strategies can be distinguished: focusing on prevention of a secondary stroke, adherence to exercises, and enhancement of participation and activities of daily living[6]. A review has shown that adding training for these self-management strategies during stroke rehabilitation can improve activities of daily living and independence[8].

To use self-management strategies, patient activation is a prerequisite[9]. Patient activation is defined as one's role in the care process and having the knowledge, skills, and confidence to manage one's health and health care. A review demonstrated that patients with chronic conditions who are more activated have better health outcomes and better care experiences than those who are less activated. However, patients with stroke were not included[10].

Until now, there was only 1 questionnaire that measures patient activation: the Patient Activation Measure (PAM)[11]. The PAM distinguishes passive patients who experience no influence on their health from active patients who do experience this influence.

Although having a sufficient level of activation is important for patients with stroke, research on this topic in patients with stroke is scarce. To our knowledge, there are only a few studies done in community-based[12-15] or hospital-based[16] patients with stroke. These studies show different levels of patient activation, varying between a level where patients are disengaged and overwhelmed[16] to a level where patients are maintaining behaviours and pushing further[12].

Increasing patient activation during stroke rehabilitation is not explicitly included in stroke rehabilitation guidelines as a treatment goal[17,18]. Consequently, stroke rehabilitation is mainly aimed at improving limitations after stroke and is not specifically aimed at increasing patient activation[19]. We therefore hypothesized that patient activation does not improve or only slightly improves during and after stroke rehabilitation. Therefore, the aim of this prospective observational study is to examine patient activation at the start of the rehabilitation, and the course of patient activation up until the 6 month follow-up.

Methods

Study design

This study was part of the Stroke Cohort Outcomes of REhabilitation (SCORE) study, a cohort study in a rehabilitation facility, which started in March 2014 and ended in December 2019. This study has been described extensively elsewhere[20]. The protocol of the study is registered in the Netherlands Trial Register. This study is reported according to the STrengthening the Reporting of OBservational studies in Epidemiology guidelines[21].

Study population

Consecutive patients with stroke who received inpatient or outpatient multidisciplinary rehabilitation were invited by the rehabilitation physician to participate in the SCORE study when they (1) were 18 years or older; (2) had a first or recurrent stroke less than 6 months prior; (3) had no psychiatric disorder or dementia; and (4) were able to complete questionnaires in Dutch. After patients were checked for their eligibility, were willing to participate, and provided written informed consent, they were included in the study.

Procedure

The protocol of the study was approved by the Medical Ethics Board of the Leiden University Medical Center (NL465321.058.13).

Patients filled in questionnaires on paper or online, depending on their preference. When there was no response within 10 days, patients were contacted by telephone or e-mail, with a maximum of 2 reminders.

The PAM was added to the set of questionnaires in March 2016. Therefore, the current study comprises patients between March 2016 and December 2019 who completed the PAM at least at 1 time point. When patients had extreme changes on the PAM at different time points (ie, a maximum score of 100 at one time point and a minimum score of 0 at another time point), they were considered as outliers and excluded.

Assessments

At the start of the rehabilitation (ie, baseline) baseline characteristics and patient reported-outcome measures were collected.

Baseline characteristics

Age, sex, and type of stroke (ischemic/haemorrhagic) were extracted from the patients' medical file. A questionnaire was used to assess the level of education (6-point scale split into 3 categories according to the Dutch system, ie, low, medium, high), living situation (married or living with a partner), paid work before stroke, and the number of comorbidities (by the Dutch study on Life Situation Questionnaire[22]). Questions about lifestyle prior to stroke included smoking (≥ 1 cigarette per day), alcohol (≥2 glasses per day), and physical activity (30 minutes of moderate to intensive daily physical activity.

A nurse assessed the Barthel Index at baseline only in patients receiving inpatient rehabilitation. This is a measure of functional independence with a score ranging from 0-20, where higher scores indicate more functional independence[23].

Patient-reported outcome measures

Health-related quality of life (HRQoL) was assessed with the EuroQol 5-Dimension 3-Level (EQ-5D-3L)[24]. The EQ-5D-3L, which consists of 5 questions concerning 5 domains (ie, mobility, self-care, usual activities, pain/discomfort, anxiety/depression), leads to an index ranging from -0.33 (worst imaginable health state) to 1 (best imaginable health state). In addition, the EQ-5D-3L comprises a visual analogue scale, ranging from 0-100.

The Stroke Impact Scale (SIS)[25] was used to measure self-reported effect of stroke on the domains mobility, communication, memory and thinking, and mood and emotions. Summative scores for each domain range from 0-100, where higher scores indicate better functionality.

Patient activation

Patient activation was assessed at baseline, at 3 months and at 6-month follow-up by means of the PAM[11]. This generic measure consists of 13 items, with ratings on a 5-point Likert-type scale (disagree strongly, disagree, agree, agree strongly, and not applicable). Total scores range from 0-100, where higher scores denote higher patient activation[9].

The PAM score can be divided in 4 progressively higher activation levels. Patients at level 1 (score 0.0-47.0) may not yet understand that their role is important. Patients at level 2 (score 47.1-55.1) lack confidence and knowledge to take action. Patients at level 3 (55.2-72.4) are beginning to take action, whereas patients at level 4 (72.5-100) are proactive about health and take action to perform many recommended health behaviours[26].

The Dutch version of the PAM has shown adequate psychometric properties in people with a chronic illness[27]. In persons with neurological conditions (patients without stroke) the PAM was found to have good internal reliability and to be valid for research purposes[28].

Statistical analyses

Data were analysed with SPSS Statistics for Windows Version 22.0. Data were presented descriptively. A *p* value of .05 was considered statistically significant.

To analyze whether there were differences in baseline characteristics between patients with paired measurements on the PAM at baseline and at 6 months and patients without paired measurements, Mann–Whitney U tests, Fisher exact tests, and chi-square tests were used, where appropriate. The same tests were used to compare all patients included in the current analyses and patients who were excluded in the current analyses (because they did not complete the PAM or were outliers).

Baseline characteristics of patients at the 4 PAM levels were compared using chi-square tests and Kruskal-Wallis tests. Post hoc tests with Bonferroni correction to correct for multiple testing were performed in case of significant differences.

To evaluate the course of the PAM scores, univariate and multivariate linear mixed-model analyses were used. A random slope and intercept model with unstructured covariance structure was fitted with measurements at baseline, 3 months, and 6-month follow-up. Possible confounders, that is, age, SIS communication, SIS memory and thinking, and SIS mood and emotions, were selected based on clinical experience. When significant in the univariate analysis, the covariable was incorporated in the multivariate model. The normality assumption of the model was checked by visual inspection of the residuals.

To evaluate the course of PAM levels for individual patients, descriptive statistics were used. For patients who filled in the PAM at baseline and at 6 months, PAM levels at these time points were graphically shown in a Sankey diagram.

Results

Between March 2016 and December 2019, a total of 506 patients with stroke were included in the SCORE study (Figure 1). Of them, 28 (5.5%) were excluded from the current analyses because 26 did not complete a PAM at any time point, and 2 had a maximal PAM score of 100 at one time point and a minimal PAM score of 0 at another time point. The frequency of an ischemic stroke was lower in these excluded patients than in the included 478 patients (64.3% versus 82.1%, $p < .001$). Other characteristics were not significantly different between these groups (results not shown).

Figure 1. Flowchart of patients with stroke included in the study between March 2016 and December 2019.

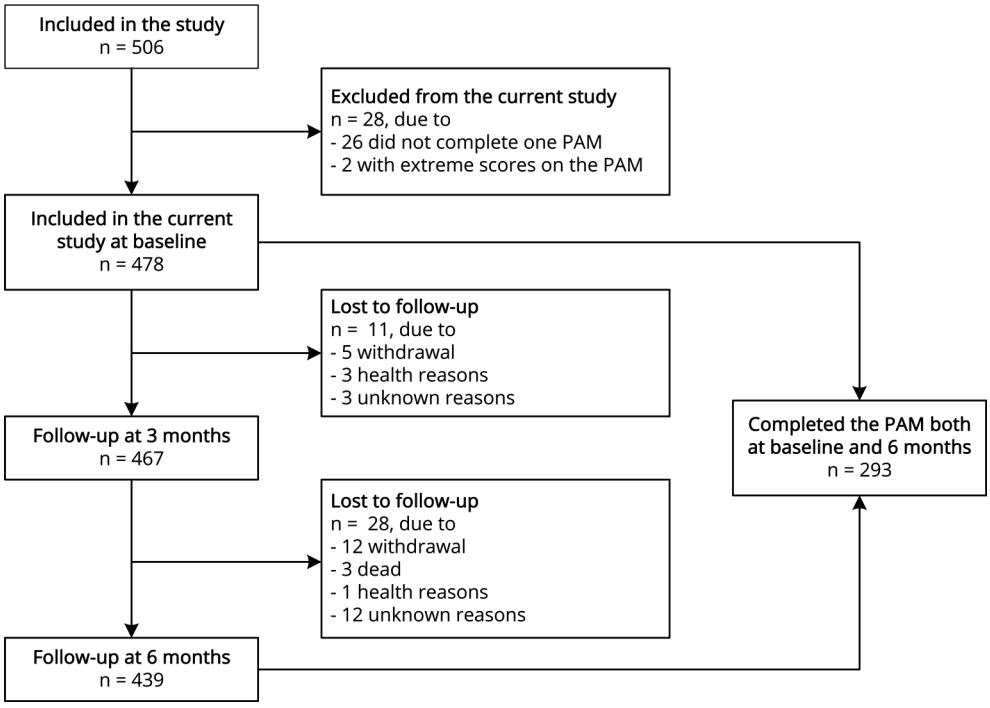


Table 1. Baseline and clinical characteristics and patient-reported outcome measure scores of patients with stroke included in the statistical analyses.

Characteristic	**Total Group Included in Analyses** (n = 478)		**Paired Measurements on the PAM at Baseline and 6 months** (n = 293)		**No Paired Measurements on the PAM** (n = 185)		***p* value***
	n		n		n		
Age (y), median (IQR)	477	63.0 (56.0-70.0)	293	64.0 (57.0-70.0)	184	62.0 (53.0-69.0)	**.041**
Men, n (%)	478	306 (64.0)	293	186 (63.5)	185	120 (64.9)	.770
Education, n (%)	469		292		177		.340
Low		197 (42.0)		128 (43.8)		69 (39.0)	
Medium		134 (28.6)		85 (29.1)		49 (27.7)	
High		138 (29.4)		79 (27.1)		59 (33.3)	
Married or living with a partner, n (%)	466	285 (61.2)	290	188 (64.8)	176	97 (55.1)	**.040**
Paid work before stroke, n (%)[†]	258	193 (74.8)	155	115 (74.2)	113	85 (75.2)	.888
No. of comorbidities, median (IQR)	392	2.0 (1.0-3.0)	249	2.0 (1.0-3.0)	143	2.0 (1.0-3.0)	.638
Smoking ≥1cigarettes/d prestroke, n (%)	465	155 (33.3)	287	80 (27.9)	178	75 (42.1)	**.002**
Alcohol ≥2 glasses/d prestroke, n (%)	458	48 (10.5)	283	28 (9.9)	175	20 (11.4)	.639
Physically active, n (%)	457	151 (33.0)	286	89 (31.1)	171	62 (36.3)	.261
Ischemic stroke, n (%)	475	390 (82.1)	293	241 (82.3)	182	149 (81.9)	.903
Inpatient rehabilitation, n (%)	478	379 (79.3)	293	226 (77.1)	185	153 (82.7)	.165
Barthel Index, median (IQR)[‡]	309	17.0 (12.0-19.0)	191	17.0 (12.0-19.0)	118	16.5 (10.0-18.0)	.115
HRQoL EQ-5D-3L index, median (IQR)	434	0.78 (0.56-0.86)	282	0.78 (0.57-0.89)	152	0.76 (0.52-0.86)	.112
HRQoL EQ-5D-3L VAS, median (IQR)	442	66.0 (50.0-80.0)	287	66.0 (50.0-80.0)	155	65.0 (50.0-80.0)	.405
SIS mobility, median (IQR)	445	83.3 (53.9-97.2)	289	83.3 (60.9-97.2)	156	77.8 (38.9-94.4)	**.013**
SIS communication, median (IQR)	450	92.9 (75.0-100.0)	290	92.9 (78.6-100.0)	160	92.9 (75.0-100.0)	.902
SIS memory and thinking, median (IQR)	450	85.7 (67.9-96.4)	289	85.7 (71.4-96.4)	161	85.7 (67.9-96.4)	.579
SIS mood and emotions, median (IQR)	449	77.8 (66.7-88.9)	290	77.8 (66.7-88.9)	159	77.8 (66.7-88.9)	.775

Abbreviations: HRQoL, health-related quality of life; SIS, stroke impact scale; VAS, visual analogue scale.
**P* values of comparison between patients who completed the PAM at baseline and 6 mo and patients without paired measurement on the PAM. Mann–Whitney *U* tests for continuous variables, Fisher Exact tests for ordinal variables and χ^2 tests for dichotomous variables, where appropriate.
[†] Only for patients aged <66 y.
[‡] Only for inpatients.

Table 1 shows the characteristics and patient-reported outcome measure scores of all included patients. Median age of all 478 patients was 63.0 years (interquartile range [IQR], 56.0-70.0 years) and 306 of them (64.0%) were men. The 293 patients with paired measurements on the PAM at baseline and at 6 months were significantly older (median, 64.0 years [IQR, 57.0-70.0 years] vs median, 62.0 years [IQR, 53.0-69.0 years], $p = .041$), were more often married or living with a partner (188 [64.8%] vs 97 [55.1%], $p = .040$), were smoking less often (80 [27.9%] vs 75 [42.1%], $p = .002$) and had a higher score for mobility (median, 83.3 [IQR 60.9-97.2] vs median, 77.8 [IQR 38.9-94.4], $p = .013$) than the 185 patients who did not have paired measurements on the PAM at baseline and at 6 months.

PAM scores and levels at baseline

At baseline 426 patients completed the PAM with a mean score of 60.2±14.3. In the 4 levels, 75 patients (17.6%) were in level 1, 85 (20.0%) in level 2, 177 (41.5%) in level 3 and 89 (20.9%) in level 4 (Table 2). Between the patients at the different levels, there were significant differences at baseline in age ($p = .040$), number of comorbidities ($p = .016$), HRQoL (EQ-5D-3L index $p < .001$ and visual analog scale $p = .001$), communication ($p = .007$), memory and thinking ($p < .001$), and mood and emotions ($p < .001$). The results of the post hoc analyses indicate more comorbidities, lower HRQoL, lower SIS communication, lower SIS memory and thinking, and lower SIS mood and emotions in patients in level 1 than patients in level 4 (all $p < .05$) (Table 2).

Table 2. Baseline characteristics of patients of each PAM level.

Characteristic	Level 1 n = 75 PAM 43.4 (3.9)		Level 2 n = 85 PAM 51.2 (1.7)		Level 3 n = 177 PAM 60.3 (4.7)		Level 4 n = 89 PAM 82.9 (9.4)		*p* value*
	n		n		n		n		
Age (y), median (IQR)	75	61.0 (53.0-66.0)	85	64.0 (55.0-69.5)	177	64.0 (57.0-70.0)	88	64.5 (56.0-70.8)	**.040**[†]
Men, n (%)	75	40 (53.3)	85	56 (65.9)	177	119 (67.2)	89	58 (65.2)	.196
Education, n (%)	74		84		176		88		.356
Low		36 (48.6)		40 (47.6)		72 (40.9)		32 (36.4)	
Medium		19 (25.7)		26 (31.0)		45 (25.6)		26 (29.5)	
High		19 (25.7)		18 (21.4)		59 (33.5)		30 (34.1)	
Married or living with a partner, n (%)	73	38 (52.1)	84	45 (53.6)	173	114 (65.9)	88	58 (65.9)	.071
Paid work before stroke, n (%)[‡]	53	36 (67.9)	43	33 (76.7)	93	66 (71.0)	46	39 (84.8)	.220
No. of comorbidities, median (IQR)	58	2.0 (2.0-4.0)	68	2.0 (1.0-3.0)	144	2.0 (1.0-3.0)	82	2.0 (1.0-3.0)	**.016**[§]
Smoking ≥1cigarettes/d prestroke, n (%)	74	25 (33.8)	82	34 (41.5)	172	56 (32.6)	88	29 (33.0)	.542
Alcohol ≥2 glasses/d prestroke, n (%)	74	8 (10.8)	81	10 (12.3)	170	21 (12.4)	86	7 (8.1)	.764
Physically active, n (%)	73	26 (35.6)	81	25 (30.9)	169	56 (33.1)	85	26 (30.6)	.898
Ischemic stroke, n (%)	75	61 (81.3)	83	64 (77.1)	176	153 (86.9)	89	72 (80.9)	.229
Inpatient rehabilitation, n (%)	75	56 (74.7)	85	67 (78.8)	177	144 (81.4)	89	67 (75.3)	.562
Barthel Index, median (IQR)[‖]	48	15.0 (10.0-18.0)	53	16.0 (11.0-18.0)	118	18.0 (12.0-20.0)	56	17.0 (11.3-19.0)	.139
HRQoL EQ-5D-3L index, median (IQR)	70	0.59 (0.39-0.78)	80	0.73 (0.52-0.86)	173	0.78 (0.64-0.90)	85	0.81 (0.66-0.90)	**<.001**[¶]
HRQoL EQ-5D-3L VAS, median (IQR)	73	0.77 (0.59-0.86)	84	0.77 (0.62-0.89)	170	0.86 (0.72-0.93)	86	0.86 (0.74-0.93)	**.001**[#]
SIS mobility, median (IQR)	74	77.8 (51.4-94.4)	83	80.6 (58.3-93.8)	172	86.8 (61.1-97.2)	89	83.3 (54.2-100.0)	.257
SIS communication, median (IQR)	73	85.7 (71.4-96.4)	85	91.7 (71.4-100.0)	175	92.9 (78.6-100.0)	87	96.4 (82.1-100.0)	**.007**[**]
SIS memory and thinking, median (IQR)	74	78.6 (60.7-92.9)	85	82.1 (67.9-92.9)	175	85.7 (67.9-96.4)	87	92.9 (78.6-100.0)	**<.001**[††]
SIS mood and emotions, median (IQR)	75	72.2 (58.3-81.3)	85	75.0 (63.9-82.7)	176	80.6 (66.7-88.9)	87	83.3 (72.2-88.9)	**<.001**[‡‡]

Abbreviations: HRQoL, health-related quality of life; SIS, stroke impact scale; VAS, visual analogue scale.

**P* values are given of Kruskall-Wallis and Chi² tests, where appropriate.
[†] Only for patients aged <66 y.
[‖] Only administered for inpatients.

Post-hoc comparison: significant difference between [†]PAM levels 1 and 3 ($p = .036$)
[§] PAM levels 1 and 4 ($p = .013$)
[¶] PAM levels 1 and 2 ($p = 0.038$), 1 and 3 ($p < .001$), and 1 and 4 ($p < .001$)
[#] PAM levels 1 and 3 ($p = .020$), 1 and 4 ($p = .010$), 2 and 3 ($p = .049$), and 2 and 4 ($p = .025$)
[**] PAM levels 1 and 4 ($p = .004$)
[††] PAM levels 1 and 3 ($p = .026$), 1 and 4 ($p < .001$), and 2 and 4 ($p = .011$)
[‡‡] PAM levels 1 and 3 ($p < .001$), 1 and 4 ($p < .001$), 2 and 3 ($p = .018$), and 2 and 4 ($p = .001$).

Table 3. PAM for patients with stroke who received rehabilitation at baseline and 3- and 6-month follow-up.

PAM		n	Baseline	n	3 Months	n	6 Months
PAM score, mean ± SD		426	60.2±14.3	367	60.7±14.8	335	61.9±18.0
PAM levels, n (%)		426		367		335	
	1		75 (17.6)		57 (15.5)		52 (15.5)
	2		85 (20.0)		77 (21.0)		68 (20.3)
	3		177 (41.5)		157 (42.8)		128 (38.2)
	4		89 (20.9)		76 (20.7)		87 (26.0)

PAM scores over time

At 3 month follow-up, 367 patients completed the PAM with a mean score of 60.7±14.8 and at 6 months 335 patients had a mean score of 61.9±18.0 (Table 3). In the univariate analysis, the PAM score did not significantly improve over time (β=0.80; 95% Confidence Interval (CI), -0.14 to 1.73; p = .094) (Table 4). Further analysis of the significantly related covariates showed that old age and worse communication, memory and thinking and mood and emotions had a negative effect on the PAM score as a function of time. In the multivariate analysis, including the significant related covariates, the PAM score did improve over time (β=7.85; CI, 2.17 to 13.52; p = .007) (see Table 4). Only higher mood and emotions remained significantly related with higher PAM scores (β=0.19; CI, 0.10 to 0.27; p < .001). Old age had a negative effect on improvement over time (β =-0.11; CI, -0.20 to -0.02; p = .016).

Table 4. PAM comparison for patients with stroke who received rehabilitation between baseline and 3- and 6-month follow-up.

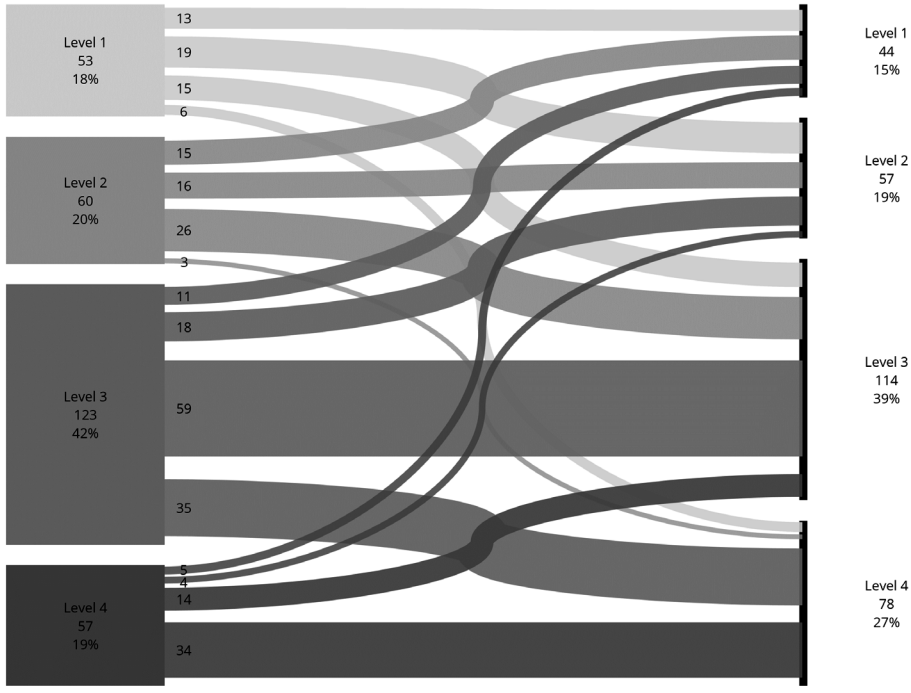
Variable	β (CI)	*p* value*
Univariate mixed-model analyses		
Time	0.80 (-0.14 to 1.73)	.094
Multivariate mixed-model analyses		
Time	7.85 (2.17 to 13.52)	**.007**
SIS communication	0.02 (-0.08 to 0.12)	.703
SIS memory and thinking	0.07 (-0.01 to 0.15)	.079
SIS mood and emotions	0.19 (0.10 to 0.27)	**<.001**
Age	0.04 (-0.07 to 0.15)	.504
Age x time	-0.11 (-0.20 to -0.02)	**.016**

* *P* value of linear mixed model.

Course of PAM levels

The course of PAM levels is visualized in Figure 2. From baseline up until 6 months, 122 patients (41.6%) remained at the same level. Of these patients, 13 (10.7%) remained in level 1 and 16 (13.1%) remained in level 2. There were 104 patients (35.5%) who improved in PAM level: 80 improved 1 level and 24 improved 2 levels or more. On the other hand, 67 patients (23.1%) decreased in PAM level: 47 decreased 1 level and 20 decreased 2 levels or more.

Figure 2. Sankey diagram of PAM levels of patients with stroke who received rehabilitation with paired measurements at baseline and 6 mo (n=293).



Discussion

This study showed that on a group level PAM scores in patients with stroke increased from the start of the rehabilitation up until the 6-month follow-up in multivariate analysis. At the individual level, 104 patients (35.5%) improved 1 or 2 PAM levels. However, the overall mean change in PAM scores was small and no significant increase in PAM score was found in the univariate analysis. At the individual level, one-third of patients were in level 1 or 2 of patient activation at all time points, and 23.1% of patients decreased in PAM level. These results are in line with our hypothesis that patient activation would not or only slightly improve during and after stroke rehabilitation.

The mean PAM score at baseline of the patients with stroke in the present study is in the same range as PAM scores in three other studies with community-based patients with stroke (60.2 versus 56.4-65.7)[13-15]. Moreover, the mean PAM score in the present study was much lower than the mean score (75.3) of stroke patients in the study of Kidd et al.[12]. The authors stated that patient activation was probably lower based on interviews with these patients[12]. In contrast, the mean PAM score in the present study was higher than in a cross-sectional study with patients with stroke from a tertiary hospital (60.2 versus 51.56)[16]. The authors hypothesized that this low patient activation might be because of underdeveloped health literacy and health care awareness[16].

A strength of this study is that it gives insight in the course of patient activation in patients with stroke during the first 3 months after stroke when most recovery takes place[29] and also up until 6 months when it is thought that a plateau effect is reached[29]. Another strength of our study is that PAM levels are described. This information at the individual patient level of knowledge and skill to self-manage allows physicians and therapists to target self-care education and provide support for each patient's needs while presumably being more effective in supporting patient's self-management[9].

Previous studies found that a low level of patient activation was associated with low income, using less preventive screening measures (eg, health screening), unhealthy behaviours (eg, smoking), worse clinical indicators (eg, systolic blood pressure), more visits to the emergency department, more admissions to the hospital[30], and more unmet medical needs and inappropriate use of the health care system[31]. In contrast to these previous studies, patients in PAM level 1 did not report significantly more unhealthy behaviours prestroke. However, they did have more comorbidities than patients in PAM level 4. Moreover, patients in level 1 had lower HRQoL, lower self-rated communication, memory and thinking, and mood and emotions compared than patients in level 4. In other words, patients who are more severely affected by their stroke, have a lower level of patient activation.

Furthermore, the number of patients with a low level of activation (level 1 and 2) was >35% at all time points. In addition, the PAM score decreased markedly in a number of patients over time. This subgroup of patients may specifically need attention and support. For patients with a low level of activation, it could be of value to introduce a tailored intervention on those aspects of patient activation that they have difficulty with. In case the level of activation of patients in level 1 does not improve, the care they receive might be more directed to compensation strategies. Patients in level 2 and 3 might benefit from interventions targeted at patient activation as a part of rehabilitation. Interventions were proven to be effective in increasing patient activation in patients with diabetes and other chronic conditions, and the highest increase was seen in patients with the lowest activation levels[10,32]. In patients with stroke, 3 different interventions were studied, which aimed at improving patient activation[13-15]. Of the 3 only 1 was significantly effective[15]. This intervention was a home-based social worker–led case management program

combined with a website providing stroke-related information. However, the exact mechanisms remain uncertain[15]. These interventions have not yet been tested in more affected patients with stroke who receive rehabilitation. This should be addressed in future research.

Study limitations

Because the PAM has not yet been validated specifically in patients with stroke, this can be considered a limitation of this study. Based on our data and 2 previous studies[12,28], there is some doubt regarding the content validity of the PAM, that is, the degree to which the content of an instrument is an adequate reflection of the construct to be measured, looking at relevance of the items, as well as comprehensiveness and comprehensibility[33]. In our study, 2 patients (0.4%) had a maximum score of 100 and a minimum score of 0 at another time point, and 11 patients (3.8%) increased or decreased 3 levels between baseline and after 6 months. It is unclear whether these patients were truly differently activated or whether there was a problem with comprehensibility because of cognitive or communicative limitations. These doubts are further substantiated by the study of Kidd et al.[12], where there seemed differences in patient activation described by PAM scores and interviews, and a study done in a population with neurologic conditions which showed that individual activation levels were underestimated due to differences in item difficulties[28]. This advocates for validation of the PAM in a population of patients with stroke who receive rehabilitation. Because the minimal important change of the PAM in patients with stroke is unknown, it was not possible to interpret whether the slight improvement observed in the present study is perceived as an important change by stroke patients. This advocates for determining the minimal important change of the PAM in patients with stroke.

A larger percentage of patients with haemorrhagic stroke were excluded from our analysis. Although the percentage of excluded patients was low (5.5%), we cannot preclude that this could have influenced the generalisability of our results. Furthermore, the 293 patients with paired measurements on the PAM at baseline and at 6 months differed significantly from the 185 who did not have paired measurements on age, living situation, smoking and mobility. Therefore, the course of PAM levels might not be generalizable to the whole population.

Conclusions

The mean PAM score in patients with stroke increased over time but only slightly. Moreover, about one-third of patients remained at low levels of patient activation, and patients decreased in their level of patient activation. This indicates that there is room for improvement because no specific interventions for increasing patient activation are part of current rehabilitation treatment. Further research is needed to determine the effectiveness of interventions to improve patient activation for this specific population.

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Chapter 6

Caregiver burden after stroke: changes over time?

Pont W | Groeneveld IF | Arwert HJ | Meesters JJL |
Rambaran Mishre AD| Vliet Vlieland TPM | Goossens PH|
on behalf of the SCORE study group.

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Abstract

Introduction and aim

Many caregivers of stroke patients experience a high burden. This study aims to describe the course of burden in individual caregivers in the first year after stroke.

Methods

This study is part of the Stroke Cohort Outcomes of REhabilitation study, a multicentre, longitudinal cohort study including consecutive stroke patients admitted to two rehabilitation facilities. Caregivers were asked to complete the Caregiver Strain Index and questions on their sociodemographic characteristics 6 and 12 months post admission. Patients' sociodemographic and clinical characteristics were extracted from medical records.

Results

A total of 129 caregivers were included, 72 completed the Caregiver Strain Index twice. Of them 19 (26.4%) were men, median age 59 (range 27-78) years. A consistently high or low burden was reported by 15 (20.8%) and 49 (68.1%), respectively, whereas 8 (11.1%) reported a high burden at either 6 (n = 3) or 12 months (n = 5).

Discussion

In the majority of caregivers of stroke patients the perceived caregiver burden is consistent over time. However, as in 11.1% caregiver burden changes from 6 to 12 months, caregiver burden should be measured repeatedly until 12 months after stroke. Caregivers living together with a patient who suffered a haemorrhagic stroke seem to be more at risk for a high burden.

Introduction

Worldwide 15 million people suffer a stroke each year[1]. Of all patients who survive the acute phase of stroke (62% after 1 year), the majority (80%) remains to some extent physically or cognitively impaired and needs help from professionals and/or caregivers[2,3]. Caregiving can be defined as task-oriented assistance provided by individuals, usually family or friends[4], with this assistance not being part of formal community support services. At 12 months post stroke 69% of first-ever stroke patients in Australia received informal care from a caregiver[5]. On the longer term, over a third of all patients were found to be dependent on others in Australia and the UK[6,7]. A South African study in community-dwelling stroke patients found that 6 months post stroke according to the Nottingham Extended Activities of Daily Living scale, many participants were dependent in housework (60.9%), food preparation (52.2%), shopping (80.4%) and the use of public transport (65.2%), suggesting the need for caregiver assistance[7].

Caring for a family member takes time as well as physical and emotional efforts[8]. Caregiving is often experienced as a burden[9-11] and can thereby lead to anxiety[12] or depressive symptoms in caregivers[2,3,8,13]. Caregiver burden is a term used to describe the weight or load carried by caregivers as a result of caring for their relative[9]. It can be divided into a subjective and objective burden. Objective burden refers to the physical assistance provided by caregivers. Subjective burden refers to the psychological, social, and emotional impact on caregivers as a consequence of objective burden[9].

The proportion of caregivers of stroke patients experiencing significant burden at a certain point ranges from 25% (moderate or considerable burden on nine or more items on the Relatives Stress Scale in two Norwegian studies with 68 and 36 caregivers, respectively, at 6 months post stroke)[14,15] to 54% (total score on the Caregiver Strain Index (CSI) ≥ 7 in a Dutch study with 187 caregivers 1 year post stroke)[16]. There are numerous instruments available to measure caregiver burden, of which the Caregiver Strain Index[17], the Caregivers Burden Scale[18], the Caregiver Reaction Assessment[19], the Sense of Competence Questionnaire[20], the Relatives Stress Scale[21], and the Zarit Burden Interview[22] are most frequently cited[23]. A study comparing the CSI, Sense of Competence Questionnaire, and Caregiver Reaction Assessment in caregivers of stroke patients found that the CSI proved to be more feasible and at least as valid as the longer and more complex Sense of Competence Questionnaire and Caregiver Reaction Assessment[24]. For the CSI validation studies specifically in stroke patients show good reproducibility (k 0.93, CI 0.84-0.97) (25) and high reliability with a Cronbach's α of 0.83[26]. On the basis of a review on measures used to assess burden among caregivers of stroke patients the CSI is recommended in Dutch guidelines on the measurement of stroke outcomes[26,27].

Regarding the course of caregiver burden over time as measured with the CSI, in multiple studies no significant changes of the average CSI score over time were found[8,28-30]. However, two longer-term follow-up studies showed that 3 and 5 years after admission to a neurological department or inpatient rehabilitation facility caregiver burden of stroke patients significantly declined[10,31]. However, if proportions of caregivers under considerable burden are considered, in longitudinal studies using the CSI one study showed an increase in the prevalence of caregiver burden over time[32], whereas four other studies did not show a change in its prevalence over time, with measurements done from 2 months post stroke until 1 year post stroke[8,28-30]. The proportions of caregivers under significant burden at specific time points varied among the studies, with 22.7% and 42.0% of caregivers reporting high burden at 12 months on the CSI[8,30].

All of these studies reported the percentages of caregivers under considerable burden over time or average scores of measures of caregiver burden but did not show the course of caregiver burden in individual caregivers. It is conceivable that caregivers who initially experience low caregiver burden experience high burden later in time and vice versa. The prevalence of high burden can be constant, whereas for individual caregivers burden could increase or decrease. It is also conceivable that caregivers with an initial low burden will be missed when the CSI is not repeated. More insight into the course of caregiver burden in individual caregivers is important. Regarding factors associated with caregiver burden in stroke, two systematic reviews on caregiver burden found patients characteristics that, although inconsistently, were related to caregiver burden, that is, age, gender, cognitive impairment, mental health, functional status, ADL dependency, and communication deficits[3,9,33]. In addition, Jaracz et al.[31] found that not only patient characteristics, but also caregiver characteristics, such as time spent caring, self-rated health, depressive symptoms, sense of coherence, and anxiety were significantly related to caregiver burden[31].

Therefore, the aims of the present study were to describe the proportions of caregivers experiencing low burden, high burden, or a change from high to low burden and vice versa at 6 months and 12 months post stroke; and to explore the patient and caregivers characteristics of caregivers with a high burden at some point in time, to make recommendations for the screening of burden of caregivers in clinical care. We hypothesized that on average general caregiver burden would remain the same over time, whereas in some individual caregivers the burden increases or decreases.

Methods

Design and setting

This study is part of the Stroke Cohort Outcomes of REhabilitation (SCORE) study; a multicentre longitudinal inception cohort study, which is currently executed in two Dutch specialized rehabilitation facilities in the western part of the Netherlands.

Multidisciplinary rehabilitation is offered to patients who have multiple and complex impairments and are expected to be discharged to their homes. Stroke patients are admitted to the rehabilitation facilities for inpatient rehabilitation if they had a recent stroke preventing the patient from living independently at home, being able to take part in at least two therapy sessions of 30 min each per day, having some learning ability, and expecting to live independently, whether or not with spouse or caregiver, with a life expectancy of at least 1 year. Patients with dementia or (neuro)psychiatric conditions do not qualify for admission. Stroke patients receive outpatient rehabilitation if they meet the same criteria, but are able to live at home.

Caregivers are actively involved in the rehabilitation process by means of meetings with the rehabilitation physician and care providers, partner courses/discussion groups, meetings with a social worker, and the possibility to join the patient during treatment[34].

The study protocol of the SCORE study was approved by the Medical Ethics Board of the Leiden University Medical Centre (LUMC), P13.249. This study is registered in the Netherlands National Trial Register (NTR) under number 4293.

Study population

We included caregivers of stroke patients who started inpatient or outpatient rehabilitation and participated in the SCORE study[34]. Stroke patients were eligible for the SCORE study if they met the admission criteria and were 18 years or older, and had a first or recurrent stroke not longer than six months ago. Exclusion criteria were being unable to complete questionnaires in Dutch or not providing written informed consent. The patients were asked whether they had a caregiver and if so, whether they agreed with inviting their caregiver. In case of agreement, they were asked to hand over an invitation letter to their caregiver, in most cases their spouse. If the patient had more than one caregiver, he or she was asked to invite the person they spent most of the time with. All caregivers willing to participate provided written informed consent. For this caregiver burden study, data from caregivers who agreed to participate in the study and who completed questionnaires on caregiver burden at 6 and/or 12 months after the start of the rehabilitation period of the stroke patient were used.

Sample size calculation

The SCORE study is collecting data that are also used in clinical practice so that a sample size calculation for the study as a whole was not deemed appropriate. To answer the particular research questions on the caregiver burden we assumed that a description of at least 100 caregivers would be needed to reflect sufficiently the potential heterogeneity in the group and allow the analysis of a limited number of factors associated with caregiver burden.

Data collection

Caregivers

Six and twelve months after the start of the rehabilitation of their nearest, the participating caregivers received a questionnaire. On the basis of the caregivers' preference, the questionnaires were sent by regular mail or by e-mail. They were asked to complete and return it within 1 week. If the caregiver did not return the questionnaire, the principle investigator (WP) called the caregiver once to remind him/her to fill in the questionnaire.

Caregiver burden

Caregiver burden was assessed using the generic CSI[17]. The CSI aims to identify problems with work, finances, and emotional burden that could rise from caregiving. It determines objective and subjective impact using 13 items with dichotomous outcome categories (yes/no). A score of 7 or more indicates a high level of burden[17].

Sociodemographic characteristics and work status

Sex, date of birth, and relation to the stroke patient (partner, parent, child, friend, sibling or other) were derived from the caregivers' consent form. At 6 months, the level of education of the caregiver was measured using a 6-point scale ("not finished primary school" to "finished university") and divided into lower, middle, and higher educated. In addition, caregivers were asked about their work status (paid employment yes or no).

Patients

Sociodemographic and clinical characteristics

Sociodemographic characteristics of the patients were derived from a questionnaire filled in at the start of the rehabilitation. Type of stroke, stroke localisation, type of rehabilitation (inpatient or outpatient), and the Barthel Index at the start of the rehabilitation were extracted from the patients' medical file. The Barthel Index is a 10-item measurement instrument that scores independence in Activities of Daily Living (ADL) and yields a score between 0 and 20, with higher scores indicating more independency[35].

Data analyses

Data analyses were performed in IBM SPSS version 22 v02 (IBM Corp: Armonk NY, 2013). The characteristics of the patients and the characteristics and CSI scores of the caregivers were presented as percentages, means, and standard deviations (SD) for normally distributed values or medians with 25-75% percentiles (interquartile range [IQR]) and minimum and maximum values for non-normally distributed variables.

For the computation of the CSI score, missing values were imputed if the missing value(s) was or were of influence on the total score being below or above the cut-off point of 7, the value(s) of the other questionnaire for that item(s) was or were imputed.

The CSI scores at 6 and 12 months for caregivers who filled in the CSI at both points in time were compared by means of the Wilcoxon signed rank test.

Characteristics of patients who did and did not provide informed consent to invite their caregiver, and of patients of whom the caregiver did and did not agree to participate in the study, were compared by means of the Mann-Whitney U test, the Fisher's exact test, or the independent samples t-test, where appropriate. The same analyses were conducted for participating caregivers who filled in the CSI at either 6 or 12 months and those who completed it at both measurement points.

Caregivers who filled in the CSI at both 6 and 12 months were divided into 4 groups. The first group consisted of caregivers with a high score (≥7) on the CSI at both 6 and 12 months (high-high), the second group consisted of caregivers with a high score on the CSI at 6 and a low score at 12 months (high-low), the third group consisted of caregivers with a low score on the CSI at 6 and a high score at 12 months (low-high), and the fourth group (low-low) consisted of caregivers with a low score on the CSI at both 6 and 12 months. The characteristics of caregivers with a high CSI score at some point in time were compared to those with a low CSI at both measurement points by means of the Mann-Whitney U test or Fisher's exact test, where appropriate.

With all statistical analyses a p values of <0.05 was considered as statistically significant.

Results

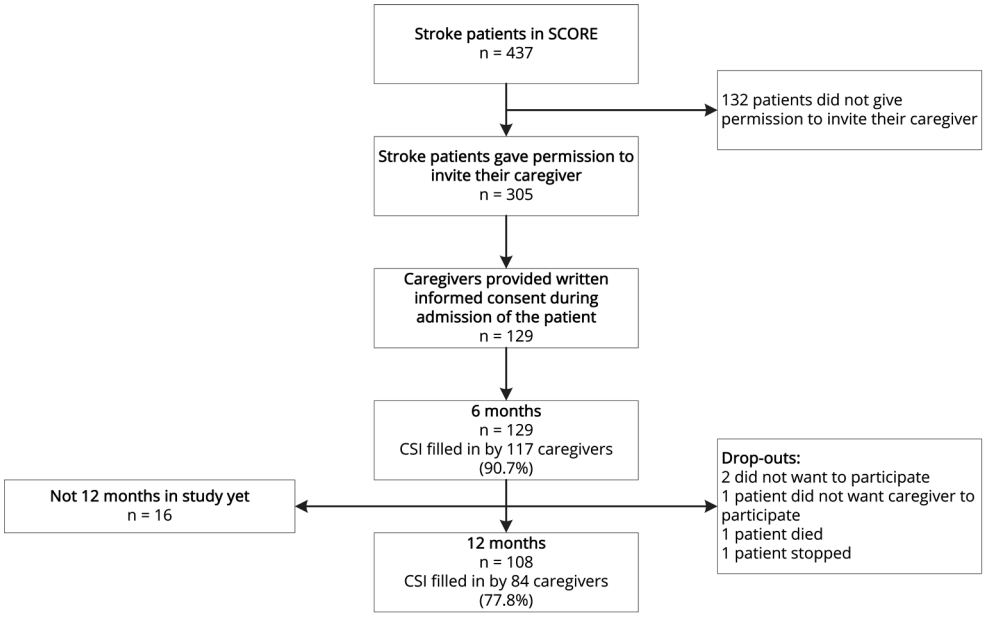
Characteristics of stroke patients and their caregivers

In the two rehabilitation facilities, ~200 and 130 stroke patients are admitted for inpatient rehabilitation per year, respectively. Counting up to 934 patients in the study period. As 339

patients of the SCORE study started in the clinic, the participation rate of clinical patients is 36%. Total number of patients immediately starting outpatient stroke rehabilitation could not be retrieved, as these data turned out to be contaminated with patients dismissed from clinical rehabilitation and follow-up consultations after termination of rehabilitation. Figure 1 displays the flow of participants in the study. Between 10 March 2014 and 1 January 2017, 436 stroke patients (~47% of the total population), admitted to inpatient or outpatient rehabilitation, provided informed consent to participate in the SCORE study. Of the patients participating in the SCORE study, 305 (70% of the SCORE population) gave permission to invite their caregiver. Patients who provided informed consent to invite their caregiver had a significantly lower Barthel Index than patients who did not provide informed consent to invite their caregiver (median 14.0, range 0.0-20.0 versus median 16.5, range 4.0-20.0; $p = 0.04$), whereas all other characteristics did not differ between these two groups (results not shown).

Of the 129 participating caregivers, 117 (90.7%) completed the CSI at 6 months, 84 (77.8%) at 12 months, and 72 (66.7%) at both time points.

Figure 1. Flow chart of caregivers of stroke patients in the SCORE-study.



Among the 305 caregivers invited, written informed consent was provided by 129 (42.3%). Table 1 shows the patient characteristics related to the caregivers who were invited and who did and did not complete one or more CSIs. In the group of patients of whom a caregiver participated in the study, significantly more patients had outpatient rehabilitation (37, 28.7%)

than in the group of whom the caregiver did not participate in the study (31, 17.6%, $p = 0.03$). None of the other patient characteristics were significantly different between the two groups.

The comparisons of the sociodemographic characteristics of the 72 caregivers who completed both CSIs versus those 57 only filling it in at 6 or 12 months, showed no significant differences between these two groups.

Table 1. Characteristics of stroke patients admitted for inpatient and outpatient rehabilitation in two rehabilitation facilities.

	Patients of whom the caregiver participated	**Patients of whom the caregiver did not participate**	***p* value**
	n = 129	n = 176	
Sex (male) (n,%)	80 (62.0)	102 (58.0)	
Age (median, [IQR, min-max])	61 (52-68; 19-68)	62 (54-69; 18-83)	
Education level (n,%)	n = 122	n = 153	
Low	55 (45.1)	64 (41.8)	
Medium	30 (24.6)	43 (28.1)	
High	37 (30.3)	46 (30.1)	
Type of stroke (ischemic) (n,%)	99 (78.6) n = 126	127 (72.2)	0.23
Stroke localisation (n,%)	n = 123	n = 171	
Left	58 (47.2)	87 (50.9)	0.50
Right	50 (40.7)	69 (40.4)	
Stem	8 (6.5)	4 (2.3)	
Posterior	5 (4.1)	7 (4.1)	
Multiple	2 (1.6)	4 (2.3)	
Inpatient rehabilitation (n,%)	92 (71.3)	145 (82.4)	**0.03**
Barthel Index (median, [IQR, min-max])	15 (9-18; 1-20) n = 61	13 (9-18; 0-20) n = 123	0.56

p Values of Mann-Whitney U test or Fisher's Exact Test, comparison of patient characteristics.

CSI: Caregiver Strain Index; SD: Standard Deviation; IQR: inter quartile range.

Caregiver burden

In 14 of the 117 (12.0%) CSIs at 6 months and 9 out of 84 (10.7%) CSIs at 12 months 1 to 3 items were missing. In all but two cases the missing values had no influence on whether a caregiver would have a total score on the CSI below or above 7. For two caregivers, the values of the previous questionnaire were imputed.

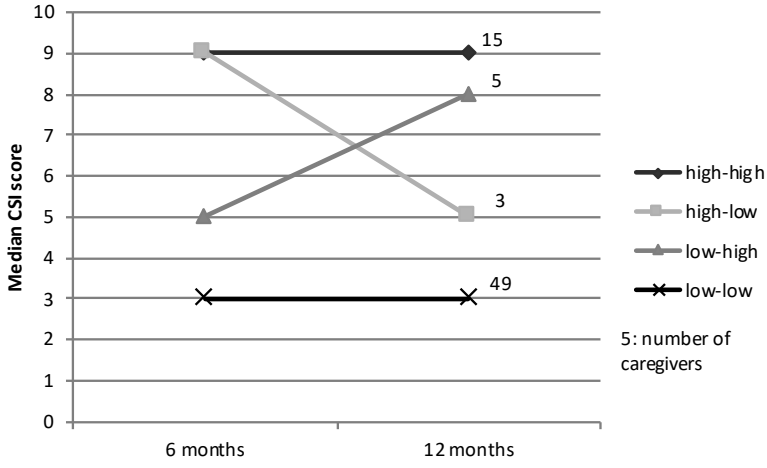
Overall, the median CSI scores at 6 or 12 months of caregivers completing the CSI twice were in the same range as those from caregivers completing at only at 6 or 12 months. Within the group of 72 caregivers completing the CSI twice, there was no significant difference between

the median scores on the CSI at 6 and 12 months. The proportions of caregivers with a high CSI score and the CSI scores at 6 and 12 months did not differ significantly in the groups of caregivers completing it at both time points or only at 6 or 12 months (all $p > 0.05$).

Caregiver burden in individual caregivers over time

Figure 2 shows the median CSI scores at 6 and 12 months past admission for the caregivers divided into four groups. Fifteen caregivers (20.8%) had a consistent high level of caregiver burden over time, whereas three caregivers (4.2%) perceived a high burden at 6 months and low at 12 months, five caregivers (6.9%) had a low burden at 6 months and high at 12 months, and 49 (68.1%) had a consistent low burden.

Figure 2. Median Caregiver Strain Index scores 6 and 12 months past admission in the SCORE study for caregivers of stroke patients divided into four groups.



Because we were primarily interested in characteristics of caregivers and patients with a high score on the CSI, and because of the small group sizes, the caregivers with a high score at some point in time were joined together and compared with the group with a low score at both time points.

Table 2 shows the characteristics of the 23 (31.9%) caregivers experiencing a high burden at both or one-time point and 49 (68.1%) caregivers with a consistent low burden. Perceiving a high burden at any time point was connected to living together with the patient and a haemorrhagic nature of stroke.

Table 2. Characteristics of caregivers of stroke patients and patients among groups of caregivers with high and low levels of caregiver burden.

	All Caregivers n = 129	**Group 1: high-high, high-low or low-high** n = 23 (31.9%)	**Group 2: low-low** n = 49 (68.1%)	***p* value**
Caregiver characteristics				
Age (median, [IQR, min-max])	59 (52-68; 15-80)	55 (52-65; 46-73)	59 (49-71; 27-78)	
Sex (male) (n,%)	41 (31.8)	6 (26.1)	13 (26.5)	
Education level (n,%)	n = 121			
Low	46 (39.0)	7 (30.4)	21 (42.9)	
Medium	37 (31.4)	6 (26.1)	14 (28.6)	
High	35 (29.7)	10 (43.5)	14 (28.6)	
Relationship with patient (n,%)				
Partner	102 (79.1)	20 (87.0)	36 (73.5)	
Parent	7 (5.4)	2 (8.7)	5 (10.2)	
Child	12 (9.3)	1 (4.3)	5 (10.2)	
Friend	2 (1.6)		1 (2.0)	
Sibling	5 (3.9)		2 (4.1)	
Unknown	1 (0.8)			
Living with relative	95 (89.5)	22 (95.7)	37 (75.5)	
Paid employment	55 (46.6)	13 (56.5)	23 (46.9)	
Patient characteristics				
Age (median, [IQR, min-max])	61 (51.5-68; 19.0-68)	60 (51-66; 21-82)	61 (49-69; 19-80)	
Sex (male) (n,%)	80 (62.0)	16 (69.6)	32 (65.3)	
Education level (n,%)	n = 122	n = 21	n = 47	
Low	55 (45.1)	7 (33.3)	25 (53.2)	
Medium	30 (24.6)	5 (23.8)	10 (21.3)	
High	37 (30.3)	9 (42.9)	12 (25.5)	
Type of stroke (ischemic) (n,%)	99 (78.6) n = 126	13 (59.1) n = 22	43 (87.8)	0.01
Stroke localisation (n,%)	n = 123	n = 21	n = 48	
Left	58 (47.2)	11 (52.4)	24 (50.0)	0.86
Right	50 (40.7)	9 (42.9)	16 (33.3)	0.45
Stem	8 (6.5)	1 (4.8)	5 (10.4)	0.44
Posterior	5 (4.1)		1 (2.1)	
Both sides	2 (1.6)		2 (4.2)	
Inpatient rehabilitation	92 (71.3)	16 (69.6)	36 (73.5)	0.78
Barthel Index (median, [min-max])	15 (1.0-20.0) n = 61	8 (4-20) n = 11	16 (5-20) n = 22	0.17

IQR: inter quartile range.
p Values of Mann-Whitney U test or Fisher's Exact test, comparison of caregivers experiencing low burden or high burden at some point in time.

Discussion and conclusion

Findings

The results of the current study show that in the majority of caregivers of stroke patients who were admitted to inpatient or outpatient rehabilitation the perceived caregiver burden does not change over time, with 20.8% reporting a high burden at both 6 and 12 months. In 4.2% the burden decreases, but in 6.9% of caregivers the burden increases. Caregiver burden is subject to change, therefore it would be recommended to measure caregiver burden up to and including 12 months.

Comparison and interpretation

For the large majority of the caregivers of stroke patients (N = 64, 88.9%) the burden they experienced over time was consistent (either low or high). These results are in line with previous studies in which was found that caregiver burden at 6 months or 1 year post stroke can be predicted based on the caregiver burden at 2 or 3 months post stoke[8,30]. The added value of the present study is that there is more insight in the course of individual burden over time. In only a small proportion of caregivers (6.3%) the burden increased over time, nevertheless this percentage is clinically relevant. It indicates that even if at 6 months a caregiver is not reaching the cut-off value for considerable strain, the considerable strain may develop over time so that all caregivers should be followed up. Extra attention should be given to caregivers living together with the patient who had a haemorrhagic stroke, because all of the caregivers for whom burden increased were living with the patient and 80% of the patients had a haemorrhagic stroke.

In the present study on average, no significant change in caregiver burden was found in the first year post stroke. However, previous longer-term follow-up studies 3 and 5 years after admission to a neurological department or inpatient rehabilitation facility showed that caregiver burden significantly declined[10,31]. It could be hypothesized that it takes more than one year for caregivers to adjust to the new situation and find ways to cope with the change in the patients' health and the changed situation[10].

Kruithof et al.[8] studied caregiver burden from the hospital to different discharge destinations. At 12 months post stroke, they found a lower percentage of high burden in the total population (22.7%), but a higher percentage for caregivers of patients discharged to a rehabilitation facility (42.5%) than we did 12 months post admission to the rehabilitation facility (30,9%)[8]. The difference may be explained by the fact that our population was not hospital-based but rehabilitation facility based, probably selecting patients with a more severe condition. Moreover, because our sample also included outpatients, the severity of impairments and

level of dependency may have been lower than in their sample of inpatients only. Previous studies showing that partners of patients who were discharged home experienced less burden than partners of patients discharged to a rehabilitation centre or nursing home confirm this hypothesis[8,36].

One might postulate that caregivers living together with the patient spend more time with actually assisting the patients with daily tasks. Indeed in the literature, it is reported in an Australian study, including 71 caregivers that at 6 months post stroke 61% of caregivers of stroke patients spend on average 4.6h helping the patient with basic and instrumental activities of daily living and household per day[29]. At 12 months the same group of caregivers spend 3.6h per day helping stroke patients[29]. This direct support is probably less in caregivers who do not live with the patients. In addition, there may be the additional burden of the changes or losses in the intimate relationship with one's spouse or partner. Given our findings, it would be interesting to focus on the difference between caregivers who do and do not live together with the patient in future research.

In the present study, it was also found that caregivers of patients with a non-ischemic nature of stroke experienced a high burden. Some previous studies did not include the nature of stroke in analyses of factors associated with high caregiver burden[10,16]. One study showed that haemorrhagic stroke is not significantly associated with high caregiver burden[36]. Another study showed that infarction is not related to burden at 2 months and 2 years post stroke[8]. A larger sample size and multivariate analyses are needed for better investigation of factors associated with high caregiver burden.

Strengths and limitations

A strength of this study is that it does not only describes the number of caregivers under considerable burden at specific time points but also whether caregivers shifted from low to high burden and vice versa over time.

A weakness of this study was the relatively small groups of caregivers, in particular, those with two completed CSI questionnaires. Among those, the groups of caregivers who experienced an increasing or decreasing burden were very small and therefore we were unable to find significant differences among subgroups. One of our main concerns was that caregivers with highest burden would not participate. For those not providing informed consent, this does not seem to be the case, as the Barthel Index of the corresponding patients was significantly higher (indicating less need of help) than that of those willing to participate. Besides, of the caregivers who did participate drop-out levels were relatively low. At 6 and 12 months past admission, 90.7% and 77.8% of the participants filled in the questionnaire, respectively.

Of the total population of stroke patients admitted for clinical rehabilitation, 36% participated in the SCORE-study. Of the SCORE-population, 70% gave permission to invite their caregiver. Patients who did and did not give permission to invite their caregiver did not significantly differ, apart from the observation that patients who gave permission to invite their caregiver were more dependent in ADL (as indicated by a lower Barthel Index) than patients who did not. Therefore, the results of the present study might not be applicable to caregivers of ADL independent patients.

Another limitation is that within the group of caregivers with a low burden, caregivers could also have experienced an increasing burden, even though they did not exceed the cut-off point of 7. In the present study, these caregivers with increasing burden were not identified.

Lastly, in the present study, we did not include the patients' (physical or mental) health status as a possible explanation for increasing caregiver burden. Several studies have been done where caregiver burden appeared related to patient outcomes[9]. However, caregiver burden has also been described to be predicted by caregiver characteristics[31]. In future studies on the course of caregiver burden, it might be interesting to include patient health outcomes as well.

Conclusions

The CSI score at 6 months is a good predictor for the score at 12 months. However, as in some caregivers, the high burden is not yet present at 6 months, monitoring caregiver burden throughout the first year after stroke seems warranted. Caregivers living together with a patient who suffered a haemorrhagic stroke seem to be more at risk for a high burden.

Implications for Rehabilitation

- Many caregivers of stroke patients experience a high burden.
- The Caregiver Strain Index score at 6 months is a good predictor for the score at 12 months.
- In some caregivers the high burden is not yet present at 6 months, therefore monitoring caregiver strain throughout the first year after stroke seems warranted.
- Caregivers living together with a patient that suffered an haemorrhagic stroke seem to be more at risk for a high burden.

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Chapter 7

Societal burden of stroke rehabilitation: costs and health outcomes after admission to stroke rehabilitation

van Meijeren-Pont W | Tamminga SJ | Goossens PH | Groeneveld IF | Arwert HJ | Meesters JJL |Rambaran Mishre AD | Vliet Vlieland TPM | van den Hout WB| on behalf of the SCORE study group

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Abstract

Objective

To estimate societal costs and changes in health-related quality of life in stroke patients, up to one year after start of medical specialist rehabilitation.

Design

Observational.

Patients

Consecutive patients who received medical specialist rehabilitation in the Stroke Cohort Outcomes of REhabilitation (SCORE) study.

Methods

Participants completed questionnaires on health-related quality of life (EuroQol EQ-5D-3L), absenteeism, out-of-pocket costs and healthcare use at start and end of rehabilitation and 6 and 12 months after start. Clinical characteristics and rehabilitation costs were extracted from the medical and financial records, respectively.

Results

From 2014 to 2016 a total of 313 stroke patients completed the study. Mean age was 59 (standard deviation (SD) 12) years, 185 (59%) were male, and 244 (78%) inpatients. Mean costs for inpatient and outpatient rehabilitation were US$70,601 and US$27,473, respectively. For inpatients, utility (an expression of quality of life) increased significantly between baseline and 6 months (EQ-5D-3L 0.66 - 0.73, $p = 0.01$; visual analogue scale 0.77 - 0.82, $p < 0.001$) and between baseline and 12 months (visual analogue scale 0.77 - 0.81, $p < 0.001$).

Conclusion

One-year societal costs from after the start of rehabilitation in stroke patients were considerable. Future research should also include costs prior to rehabilitation. For inpatients, health-related quality of life, expressed in terms of utility, improved significantly over time.

Lay abstract

The objective of this study was to estimate societal costs and changes in health-related quality of life in stroke patients, up to one year after the start of rehabilitation. Participants were stroke patients who received inpatient or outpatient rehabilitation. They completed questionnaires on quality of life, absenteeism, out-of-pocket costs and healthcare use at start and end of rehabilitation and 6 and 12 months after the start of rehabilitation. Rehabilitation costs were obtained from the financial records. From 2014 to 2016 a total of 313 patients completed the study. Mean age was 59 years, 185 (59%) were male and 244 (78%) inpatients. Mean costs for inpatient and outpatient rehabilitation were $70,601 and $27,473, respectively. For inpatients, health-related quality of life increased significantly between baseline and 6 months, and between baseline and 12 months. In conclusion, societal costs one year after the start of rehabilitation were considerable and health-related quality of life improved for inpatients.

Introduction

The number of people living with stroke in Europe is expected to increase from 1.1 million per year in 2000 to 1.5 million per year in 2025. Stroke survivors may experience severe functional impairments, including impairments in physical functioning[2], cognition[3], and speech/language[4], which, in turn, lead to limitations in activities and participation and to worse quality of life (QoL)[5]. Specialist rehabilitation was proven to be effective in improving functional outcomes after stroke[6], such as motor function, balance, walking speed and activities of daily living[7-9]. Furthermore, in stroke patients admitted for inpatient rehabilitation, QoL increased significantly between admission and discharge[10].

Besides the fact that rehabilitation after stroke is effective, rehabilitation was also found to be the main contributor to the costs of post-stroke care, according to a systematic review published in 2018 including 42 publications[11]. Costs of post-stroke care, but not those of acute care, were included. Rehabilitation in different care settings was evaluated, which included primary, secondary and tertiary care, and the costs often applied to part of the patients and were not described in detail. For the delivery of value-based healthcare (VBHC), it is important to consider not only the health effects and patient-reported outcome measures, but to also evaluate the costs of care, since it is important to achieve good patient outcomes per dollar spent[12,13].

The aim of the present study was therefore: (i) to estimate the 1-year societal costs from the start of the rehabilitation in stroke patients treated in a medical specialist rehabilitation facility in the Netherlands; and (ii) to evaluate health changes in terms of utility (an expression of quality of life) over that year.

Methods

Design, setting and subjects

This study was part of the Stroke Cohort Outcomes of REhabilitation (SCORE) study; a longitudinal inception cohort study, which is executed in one secondary care rehabilitation facility with multiple locations in the Netherlands. This study has been described extensively elsewhere[14].

In the Netherlands, after a mean of 8 days of hospital admission, approximately 71% of patients are discharged home, 15% are discharged to geriatric rehabilitation, and 14% are referred to inpatient rehabilitation in a medical specialist rehabilitation facility[15]. In general, younger, pre-stroke more active patients with complex impairments are admitted to medical specialist rehabilitation compared with geriatric rehabilitation[16]. Furthermore, patients referred to

medical specialist rehabilitation want to regain a high level of participation, including return to work, family and social roles and leisure activities. Many different disciplines are involved in medical specialist rehabilitation treatment, and the rehabilitation facilities comprise, amongst others, a sports hall and a swimming pool.

Stroke patients are admitted to the rehabilitation facility for inpatient rehabilitation if they: (i) have had a recent stroke preventing the patient from living independently at home; (ii) are able to take part in at least 2 therapy sessions of 30 min each per day; (iii) are likely to benefit from rehabilitation therapy; and (iv) are expected to live independently after discharge, whether or not with spouse or caregiver. Stroke patients receive outpatient rehabilitation if they meet the same criteria, but are able to live at home. Stroke patients were eligible for the study, if they were at least 18 years old and had a first or recurrent stroke no longer than 6 months previously. Exclusion criteria were being unable to complete questionnaires in Dutch or not providing written informed consent.

This trial is registered at the Dutch Clinical Trial Registration (NL4147 at www.trialregister.nl). The study protocol of the SCORE-project was approved by the Medical Ethics Board of the Leiden University Medical Center (LUMC), P13.249, and is reported in accordance with the STROBE guidelines[17].

Assessments

Patients completed questionnaires at the start of the rehabilitation (baseline), at discharge (inpatients) or at the end of the rehabilitation (outpatients) and at 6 and 12 months after baseline. Appendix 1 shows which questionnaires were completed at the different measurement moments. Clinical characteristics and the Barthel Index (BI) were extracted from the patients' medical file. The BI is a nurse-reported 10-item measurement instrument that scores independence in activities of daily living (ADL) and yields a score between 0 and 20, with higher scores indicating more independence[18].

Of the Stroke Impact Scale (SIS)[19], patients completed the domains communication (7 items), mobility (9 items), memory and thinking (7 items) and hand functioning (5 items). Items were scored on a 1-5-point Likert scale and transformed to a score out of 100[19], with higher scores indicating a lower level of difficulty experienced with the task. Internal consistency (Cronbach's α 0.86-0.98) was found to be excellent among stroke survivors and validity was supportive[20].

Healthcare and non-healthcare costs

Societal costs were estimated from the start of the rehabilitation until one year later, separately for inpatients and outpatients. Rehabilitation costs included length of stay in the rehabilitation facility

(the number of days for which nursing care was provided) and direct hours of therapy. Volumes and unit prices were obtained from the (financial) administration of the rehabilitation facility. In the patient questionnaires at 6 and 12 months other cost items in the preceding 6 months were assessed. This included healthcare usage outside the rehabilitation facility, out-of-pocket expenses (e.g. for crutches or an electric scooter), informal care, paid home-care and absenteeism. These items were valued using reference prices obtained from the Dutch guidelines for economic evaluations in healthcare[21]. If no reference price was available, market prices were used. Absenteeism was valued using the friction costs method, which counts absenteeism for, at most, the duration of the friction period, i.e. the 12-week period considered necessary to fill a vacancy due to long-term sick leave[21]. Costs were converted to US dollars (USD) using the purchasing power parity, as listed by the Organisation for Economic Co-operation and Development (OECD) on its website, and are reported at price level 2019[22]. Appendix 1 shows the unit costs.

Health-related quality of life and utility

The patient-reported EuroQol EQ-5D-3L (23) measures health-related quality of life (HRQoL) and consists of 5 domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. A visual analogue scale (VAS) records the patient's self-rated health on a vertical scale with endpoints labelled "Best imaginable health state" and "Worst imaginable health state"[23]. Utility scores were calculated from the 5 domains using the Dutch tariff[24] and from the VAS scale. A utility or weight of one reflects complete health, whereas 0 reflects health as poor as death[25]. The EQ-5D-3L has shown reasonable validity and reliability[23,26] and moderate responsiveness[27] for patients with stroke.

Statistical analyses

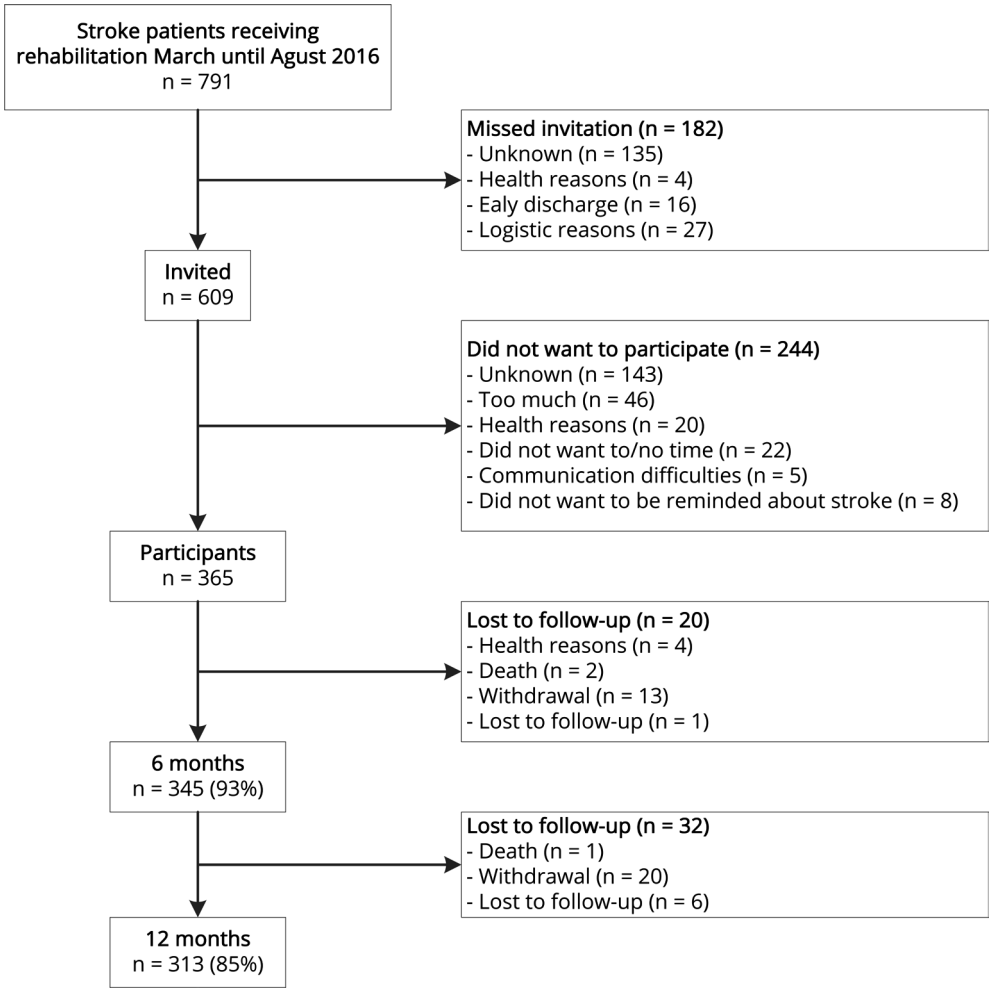
Data analyses were performed in IBM SPSS version 22 v02 (IBM Corp., Armonk, NY, USA, 2013). To account for systematic missingness, data were imputed using multiple imputation by chained equations (MICE)[28,29] with predictive mean matching[30,31] and 100 imputation sets. Missing values for out-of-pocket costs were imputed, based on either the mean price if 50% or more of the participants filled in a price, or market prices otherwise.

Characteristics of patients who did and did not agree to participate, who did and did not complete the study period and inpatients and outpatients were compared using independent-sample t-tests, Fisher's exact tests or Mann-Whitney U tests, where appropriate. Utility scores were compared using paired-sample t-tests at baseline vs 6 months, baseline vs 12 months, and 6 vs 12 months, respectively. Univariate linear regression analyses with total costs as a function of baseline utility were performed separately for inpatients and outpatients.

Results

Figure 1 shows that, between 10 March 2014 and 31 August 2016, 791 stroke patients, were admitted for inpatient or outpatient rehabilitation. Of these, 182 (23%) patients were missed and 609 (77%) patients were invited to participate. A total of 244 (40%) of the invited patients were not willing to participate. A total of 365 (60%) of the invited patients signed informed consent and completed one or more questionnaires. Sex and age did not differ significantly between patients who did and did not participate in the study (mean age 59.7 vs 60.4 years, p = 0.40; percentage male 58% vs 56%, p = 0.66, respectively).

Figure 1. Flowchart of stroke patients included in the Stroke Cohort Outcomes of REhabilitation (SCORE) study between March 2014 and August 2016.



The 12-month follow-up period was completed by 313 patients. Fifty-two patients dropped out (17%). Baseline characteristics did not differ significantly between patients who did and did not complete the study (see Table 1).

Of those who completed the study, inpatients were significantly older than outpatients (mean age 60 vs 56, $p = 0.02$). Furthermore, inpatients scored significantly better than outpatients on communication (median 92 vs 86, $p = 0.01$) and memory and thinking (median 89 vs 75, $p < 0.01$) as measured with the SIS at baseline. Outpatients had a significantly better hand function than inpatients at baseline (median 75 vs 50, $p = 0.02$).

A total of 244 (78%) patients received inpatient rehabilitation with, a median duration of 44 days (interquartile range (IQR) 14-155). Of these, 160 (61%) received outpatient rehabilitation thereafter, with a median duration of 126 days (IQR 72-186). The median duration of rehabilitation for outpatients was 105 days (IQR 70-164).

Of the baseline measurements 5% were missing. Of the QoL, absenteeism, and healthcare use measurements at baseline 12%, 38% (in patients younger than 66 years, who reported that they had paid work at baseline) and 2% were missing.

Costs

Mean total costs were US$70,601 for inpatients and $27,473 for outpatients (see Table 2). For inpatients, rehabilitation was the biggest contributor to the costs ($46,870; 66%), followed by productivity loss ($10,211; 14%) and informal care ($6,575; 9%). For outpatients, rehabilitation was also the biggest contributor ($9,899; 36%), although to a lesser extent than in inpatients, followed by productivity loss ($9,416; 34%) and informal care ($4,531; 16%).

The costs of rehabilitation therapy for inpatients were about three times higher than for outpatients ($30,741 vs $9,899). The largest contributor to the costs of rehabilitation for outpatients was physical therapy ($2,579; 26% of the total rehabilitation costs), followed by occupational therapy ($2,061; 21%) and psychology ($1,835; 19%). For inpatients the costs of stay were the largest contributor to the costs of rehabilitation ($16,129; 34%), followed by physical therapy ($7,707; 16%) and occupational therapy ($5,813; 12%).

Table 1. Characteristics of stroke patients admitted for inpatient or outpatient rehabilitation in a rehabilitation facility, completing and not completing the present study.

	n	Inpatients who completed the study	n	Outpatients who completed the study	*p* value[c] inpatients vs outpatients	n	Patients who completed the study	n	Patients who did not complete the study	*p* value[c] patients who did vs who did not complete the study
	244		69			313		52		
Sex, male, n(%)		146 (60)		39 (57)	0.62		185 (59)		28 (54)	0.54
Age, years, mean (SD)		60 (12)		56 (12)	**0.02**		59 (12)		62 (12)	0.11
Education level, n (%)					0.19					0.41
Low		109 (45)		22 (32)			131 (42)		26 (50)	
Medium		63 (26)		26 (38)			88 (28)		13 (25)	
High		72 (30)		22 (32)			94 (30)		14 (27)	
Type of stroke (ischemic), n (%)		183 (75)		57 (83)	0.20		240 (77)		41 (79)	0.71
Stroke localisation, n (%)					0.37					0.66
Left		109 (45)		38 (57)			147 (48)		26 (50)	
Right		104 (43)		22 (33)			127 (41)		21 (40)	
Other		31 (13)		9 (12)			40 (13)		5 (9)	
Rehabilitation (inpatient), n (%)							244 (78)		45 (87)	0.20
Duration inpatient rehabilitation, days, median (IQR)	39	44 (14-155)		-						
Outpatient rehabilitation after inpatient rehabilitation, n (%)	241	146 (61)		-						
Duration outpatient rehabilitation, days, median (IQR)	113	126 (72-186)	67	105 (70-164)						
Barthel Index, mean (SD)[a]		14 (5)		-	**-**		14 (4)		14 (5)	0.54
Communication (SIS)[b], median (IQR)	212	93 (79-100)	64	86 (71-93)	**0.01**	282	92 (75-100)	45	88 (73-96)	0.43
Mobility (SIS)[b], median (IQR)	37	81 (43-96)	20	92 (78-100)	0.06	57	83 (64-97)	7	58 (54-92)	0.15
Memory and thinking (SIS)[b], median (IQR)	218	89 (74-96)	64	75 (65-86)	**<0.01**	288	86 (71-96)	46	80 (63-94)	0.24
Hand function (SIS)[b,d], median (IQR)	130	50 (5-80)	20	75 (55-80)	**0.02**	150	60 (9-80)	24	40 (3-73)	0.30

[a]Scale range 1-20; higher scores denote better functioning. [b]Scale range 0-100; higher scores indicate a lower level of difficulty experienced with the task. [c]p-value of the independent samples t-test, the Fisher's exact test or the Mann-Whitney U test, where appropriate. [d]Only for patients who indicated that their hand was affected by stroke. SD: standard deviation.

Table 2. Mean resource use and costs among stroke inpatients and outpatients, in the first year after admission to a rehabilitation facility.

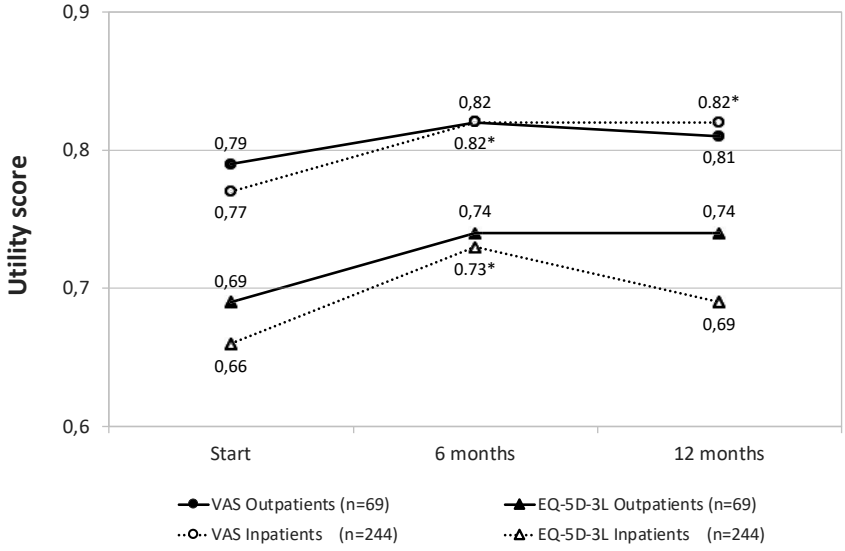
	Inpatients, n=244			**Outpatients,** n=69		
	% patients	**Volume[a]**	**Costs (US$)[b]**	**% patients**	**Volume[a]**	**Costs (in US$)[b]**
Rehabilitation						
Rehabilitation physician, h	100	10.7	4,078	100	1.9	833
Physical therapy, h	100	47.2	7,707	96	16.2	2,579
Occupational therapy, h	100	36.4	5,813	99	13.2	2,061
Speech-language therapy, h	100	18.4	3,014	70	9.2	1,073
Psychology, h	99	16.3	4,082	86	14.6	1,835
Social work, h	100	12.3	2,010	96	8.2	1,271
Recreational therapy, h	98	8.2	1,155	4	2.1	11
Other therapy, h	100	23.5	2,881	51	2.4	236
Total rehabilitation therapy, mean (SD)			30,741 (17,345)			9,899 (6,020)
Rehabilitation stay, days	100	50.0	16,129	-	-	-
Total rehabilitation, mean (SD)			46,870 (24,580)			9,899 (6,020)
Non-rehabilitation healthcare						
Hospital readmissions, days	22	15.5	2,046	16	8.2	785
General practitioner, visits	81	5.5	185	79	5.4	179
Neurologist, visits	56	2.3	158	65	2.3	186
Other medical specialists, visits	63	3.9	277	68	6.5	505
Occupational physician, visits	33	4.5	252	43	5.3	384
Allied health professionals, visits	67	32.9	1,082	52	22.0	566
Total non-rehabilitation healthcare, mean (SD)			3,999 (7,000)			2,604 (2,940)
Total healthcare costs, mean (SD)			50,869 (26,617)			12,502 (7,023)
Other non-healthcare						
Out of pocket costs, number of devices	65	4.3	2,575	28	2.4	889
Informal care, h	80	469.1	6,575	69	374.1	4,531
Paid home care, h	11	88.8	371	4	54.7	135
Productivity loss, h[c]	42	375.2	10,211	60	271.6	9,416
Total non-healthcare costs, mean (SD)			19,732 (15,267)			14,970 (12,244)
Total costs, mean (SD)			70,601 (34,534)			27,473 (15,200)

[a]Volume for patients who received care. [b]Costs for total population. [c]Productivity loss was calculated for patients under the age of 65 years who reported that they had paid work at baseline. SD: standard deviation.

Utility scores

Fig. 2 shows the utility scores over time, according to the EQ-5D-3L and the VAS. For inpatients, mean baseline utility was 0.66 (standard deviation (SD) 0.27) from the EQ-5D-3L and 0.77 (SD 0.16) from the VAS. For outpatients, mean baseline utility was 0.69 (SD 0.23) from the EQ-5D-3L and 0.79 (SD 0.15) from the VAS. For inpatients, utility improved significantly between baseline and 6 months (EQ-5D-3L, $p = 0.01$; VAS $p < 0.001$) and between baseline and 12 months (VAS, $p < 0.001$). For outpatients there was no statistically significant change over time. The decrease in utility according to the EQ-5D-3L between 6 and 12 months observed in inpatients was not statistically significant ($p = 0.11$).

Figure 2. Utility scores calculated from the EuroQoL EQ-5D-3L classification system and from the visual analogue scale (VAS), at start of rehabilitation, 6 and 12 months for stroke patients admitted to a rehabilitation facility.



*Statistically significant differences compared with start of rehabilitation.

Tables 3 and 4 show the results of the linear regression analyses with total costs as a dependent variable and utility as an independent variable. Baseline utility from the EQ-5D-3L and VAS are both significantly associated with total costs for inpatients ($p < 0.001$ for both). For outpatients baseline utility from the VAS was significantly associated with total costs ($p = 0.014$). For example, an outpatient with a baseline VAS utility score of 0.79 is expected to have total costs 58,162-38,934´0.79=27,404 USD, whereas an outpatient with a worse baseline VAS utility score of 0.49 has higher expected total costs 58,162-38,934´0.49=39,084 USD.

Table 3. Linear regression analysis of total costs as the dependent variable and utilities as independent variable, for stroke patients who received inpatient rehabilitation (n = 244) in a rehabilitation facility.

Inpatient model	Point Estimate	95% CI	*p* value
Baseline EQ-5D-3L			
Intercept	98,091	85,227 to 110,954	**<0.001**
Slope	-41,526	-59,369 to -23,682	**<0.001**
Baseline VAS			
Intercept	144,426	122,723 to 166,128	**<0.001**
Slope	-96,010	-123,616 to -68,404	**<0.001**

CI: confidence interval; VAS: visual analogue scale; EQ-5D-3L: EuroQol EQ-5D-3L.

Table 4. Linear regression analysis of total costs as the dependent variable and utilities as independent variable, for stroke patients who received outpatient rehabilitation (n = 69) in a rehabilitation facility.

Outpatient model	Point Estimate	95% CI	*p* value
Baseline EQ-5D-3L			
Intercept	29,844	17,725 to 41,964	**<0.001**
Slope	-3,408	-20,020 to 13,205	0.688
Baseline VAS			
Intercept	58,162	38,755 to 77,568	**<0.001**
Slope	-38,934	-63,115 to -14,753	**0.002**

CI: confidence interval**.**

Discussion

One-year costs after the start of medical specialist rehabilitation post stroke from a societal perspective were $70,601 and $27,473 for inpatients and outpatients, respectively. For both inpatients and outpatients, rehabilitation was the biggest contributor, yet to a larger extent in inpatients than in outpatients. Both the costs for stay in the rehabilitation facility and for all types of therapy were higher. Productivity loss and informal care were other large contributors to the costs for both inpatients and outpatients. Between baseline and 6 months, and baseline and 12 months, utility improved significantly for inpatients. A linear regression analysis showed that utility at baseline significantly predicted costs.

Communication, memory and thinking and hand function differed significantly between inpatients and outpatients in the current study. Patients with motor problems were more often admitted for inpatient rehabilitation, whereas patients with cognitive complaints more often received outpatient rehabilitation. Using the EuroQol EQ-5D-3L and VAS, significant improvements were found over time in inpatients, but not in outpatients. This could be explained by the smaller number of outpatients or, alternatively, by the fact that the EQ-5D-3L does not explicitly measure cognitive complaints, which are more prevalent among outpatients. The differences between inpatients and outpatients might also partly explain

the higher costs of rehabilitation treatment for inpatients. Since the clinical characteristics of inpatients and outpatients differ significantly at admission, it is not valid to compare outcomes in terms of utilities and costs between these groups.

Comparison with the literature

The current results are in line with a previous review, which found that rehabilitation was the main contributor to the costs of post-stroke care, followed by informal care[11]. In other studies the costs of medical interventions, physiotherapy, occupational and speech therapy, nursing care, primary care visits, readmissions to hospital due to recurrent stroke, emergency care during the rehabilitation period and other costs, such as medication, community services, transportation, meals on wheels and assistive devices, were included. Although the costs for rehabilitation found in the present study are high, research showed that the benefits for society outweigh the costs[32].

At 6 and 12 months after the start of the rehabilitation EQ-5D-3L utility scores were 0.73 and 0.69 for inpatients and 0.74 and 0.74 for outpatients. These results are mostly in line with a Dutch hospital-based study that found utility scores of 0.74 and 0.74 at 6 and 12 months post stroke, respectively[15]. The lower 0.69 utility score for inpatients at 12 months in the current study might be explained by the fact that patients referred to medical specialist rehabilitation are more severely affected by stroke than patients included in a hospital-based study[16].

Rehabilitation facilities in the Netherlands are obliged to work with national guidelines. Yet the recommendations are not very detailed, leaving room for local variation. Previous research showed that there were many similarities, but to some extent there was also some practice variation in the structure and processes of rehabilitation as delivered by rehabilitation facilities[33,34]. Variation mainly concerned patient subgroups, clinical pathways and the duration of aftercare[34]. Practice variation might lead to some difference in costs. However, differences are expected to be small, since health insurers and healthcare providers have made agreements on the price of healthcare, based on the amount of care a patient with a certain diagnosis needs on average. This is also the case for stroke rehabilitation.

Strengths and limitation

A strong point of this study is that there are not many studies on costs of medical specialist rehabilitation that include patient-reported out-of-pocket costs, absenteeism, healthcare usage and utility. Furthermore, different types of therapy during rehabilitation were estimated separately. Evaluating the costs of care is an important aspect in the delivery of value-based healthcare[12,13].

An important limitation of the present study is that the included costs started at the start of the rehabilitation. Already before the start of the rehabilitation considerable costs are incurred, for example for ambulance care, emergency care, hospital stay, magnetic resonance imaging (MRI), thrombolysis or thrombectomy. Costs in the Netherlands may also not be representative for other healthcare setting. Patient reports about absenteeism and the EQ-5D-3L contained more than 10% missing values. Multiple imputation was used to account for bias, but may not have prevented all bias.

An additional limitation was that absenteeism was self-reported, possibly leading to under-reporting of the time someone was absent[35]. Of all patients eligible for participation in this study, 54% were missed or not willing to participate. Therefore, selection bias may have occurred. Although sex and age did not differ significantly between patients who participated in the study and those who did not because they were not invited or refused participation, a limitation of this study is that we do not know whether these patients differed on other characteristics, such as functional limitations. Patients who have more functional or cognitive limitations might not have been able to participate in the study and might need more time to learn and therefore more care. The results of the regression analysis showed that patients with a worse baseline utility have higher total expected costs. Given this lack of information, it remains unclear whether the costs found in the present study could be somewhat over- or under-estimated.

Recommendations for future research

Costs prior to admission to the rehabilitation facility and costs of medication were not included in the present study. For future research it would be recommended to include these costs.

The European Stroke Organisation (ESO) Health Economics Working Group made a protocol to standardise and improve the economic evaluations of interventions for stroke. Resources mentioned in this protocol, but not included in the present study, were amongst others transport, change in residence and living arrangements, medications and more clinical outcomes after treatment[36]. Although this was not a comparative study, gathering this data on resources might help to standardize research and compare outcomes. Therefore, in future research it would be recommended to gather data on these resources.

Another recommendation for future research is to consider extracting healthcare usage outside the rehabilitation facility from a health insurer or other central administration system in order to get more complete data. Such administrative data do not rely on patients' recall, but can be difficult to obtain, and may lack the detail necessary to provide real insight[37]. Previous research on the reliability of stroke patients' reports of general practitioner visits over 12 months found that patients modestly under-reported the number of visits[38].

Conclusion

In conclusion 1 year costs from the start of medical specialist rehabilitation post stroke from a societal perspective were estimated at US$70,601 and $27,473 for inpatients and outpatients, respectively. Future research should include costs prior to the rehabilitation, since considerable costs are incurred in the acute phase. For inpatients, utility improved significantly between the start of the rehabilitation and both 6 months and 12 months.

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Appendix 1. Questionnaires completed by stroke patients and other data sources, measurement moments and unit costs.

	Source	Start of rehabilitation	Discharge/end of rehabilitation	6 Months	12 Months	Unit costs (US$)
Sociodemographic characteristics						
Sex						
Age	Patient reported	x				
Education level (low, medium, high)						
Clinical characteristics						
Type of stroke (ischemic)						
Stroke localisation (left, right, other)						
Rehabilitation (inpatient)						
Duration inpatient rehabilitation	Medical file	x	x			
Outpatient rehabilitation after inpatient rehabilitation						
Duration outpatient rehabilitation						
Barthel Index						
Stroke Impact Scale (SIS)	Patient reported	x				
Health-related quality of life and utility						
EQ-5D-3L and visual analogue scale	Patient reported	x		x	x	

	Source	Start of rehabilitation	Discharge/end of rehabilitation	6 Months	12 Months	Unit costs (US$)
Healthcare usage and costs						
Direct h of therapy rehabilitation facility (rehabilitation physician, physical therapist, sports therapist, occupational therapy, speech-language therapist, clinical linguist, psychologist, psychology assistant, psychiatrist, social work, recreational therapy, other therapy)	Administration system				x	Range 85 - 402
Length of stay rehabilitation facility	Administration system				x	326
Hospital readmissions						
General practitioner						597
Neurologist						41
Other medical specialists						124
Occupational physician	Patient reported			x	x	114
Allied health professionals (physical therapist, occupational therapist, speech and language therapist, psychologist, social worker, dietician, sexologist)						169 Range 38 – 112
Non-healthcare costs						
Out of pockets costs	Patient reported		x	x	x	
Informal care	Patient reported			x	x	18
Paid home care						
Domestic help	Patient reported			x	x	25
Care						63
Nursing						92
Productivity loss	Patient reported	x		x	x	44

Chapter 8

Summary and General Discussion

Summary

Stroke, or cerebrovascular accident is a common condition. Despite the improvement of the acute treatment of in particular ischemic stroke, it has a considerable impact on many patients' lives. Stroke can result in impairments, limitations and/or restrictions in the areas of physical, cognitive, emotional, communicative, social and societal functioning. The consequences of stroke thus not only constitute a burden for individual patients and their caregiver, but for healthcare systems and societies as a whole as well.

In order to describe, monitor and evaluate the complexity of outcomes after stroke, a comprehensive framework for health status is needed, either or not comprising specific outcome measures. The World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF) is an example of such a framework[1,2]. Specifically for stroke the ICF Core Sets for stroke were developed, covering the areas of health status most relevant for patients with stroke[2]. The Standard Set for Stroke of the International Consortium of Health Outcome Measurement (ICHOM)[3] and a Minimal Data Set (MDS) Acquired Brain Injury (ABI)[4] are alternatives, both including measurement instruments covering domains overlapping with the ICF Core Sets.

Although in stroke research there is a considerable amount of literature addressing most of the domains of health that are most relevant for patients with stroke, there are still areas where knowledge is relatively scarce. The current thesis addresses six of these knowledge gaps, focusing on the subgroup of stroke patients who receive multidisciplinary rehabilitation. Moreover, this thesis does not only focus on the subacute (rehabilitation) phase, but on the chronic phase until 30 months after stroke as well.

This thesis includes, with the exception of one study (Chapter 3), data from the Stroke Cohort Outcomes of Rehabilitation (SCORE) study, that was designed and initially executed in two rehabilitation centres, Rijnlands Rehabilitation Centre in Leiden and Sophia Rehabilitation in The Hague (currently: Basalt)[5-7]. The SCORE study had a prospective observational design, including consecutive stroke patients admitted for multidisciplinary inpatient or outpatient rehabilitation.

The research aims of the SCORE study were to describe the functions, activities, participation, and quality of life of stroke patients on the short and long-term, and to describe stroke-related costs from the perspectives of rehabilitation, healthcare, and society. This thesis addresses both of the abovementioned overarching research questions, thereby covering all four components of the ICF, i.e. upper extremity pain (Body functions and structures), functional independence and paid employment (Activities and participation), patient activation (Personal Factors), caregiver burden and healthcare usage and costs (Environmental Factors).

Chapter 1 provides a general introduction to the definition, epidemiology and clinical management of stroke, and various frameworks and sets of outcome measures capturing the complexity of its consequences.
Moreover, this chapter introduces the general aims of this thesis, being:

- to describe the long-term course of pain, participation, patient activation, caregiver burden, healthcare usage and costs and;
- to assess whether the USER or the Barthel Index can be used best to describe functional independence in stroke patients receiving rehabilitation.

Regarding the consequences of stroke on the level of the ICF component Body functions, the study presented in **Chapter 2** aimed to describe the course of the occurrence and severity of upper extremity pain in stroke patients. A total of 678 stroke patients who received multidisciplinary rehabilitation completed a question on the presence of upper extremity pain (yes/no) at three, 18 and 30 months after starting rehabilitation. If present, they rated its intensity with a visual analogue scale, ranging from 0 (i.e. no pain at all) to 10 (i.e. the worst imaginable pain). Generalized estimating equations models and linear mixed models were used to evaluate changes in proportions of patients and severity over time, respectively.
The proportions of patients reporting upper extremity pain were 260/622 (41.8%), 187/519 (36.0%) and 146/446 (32.7%), at three, 18 and 30 months respectively. This decrease in proportions over time reached statistical significance (odds ratio 0.82, 95% confidence interval (CI) 0.74-0.92, $p < 0.001$). In those reporting upper extremity pain, the median intensity was 5.0 (interquartile range (IQR) 3.0) at three and 18 months and 5.0 (IQR 4.0) at 30 months, respectively. In the 73 patients who reported pain at all time points, the median pain intensity scores were in the same range, with no significant changes over time (β -0.22, CI -0.46-0.01, $p = 0.06$). In other words, the proportion of patients reporting upper extremity pain after stroke is considerable, despite a significant decrease from 41.8% to 32.7% over a period of 2.5 years. In those reporting pain, the intensity did not change over time. These results suggest that there is need for improvement of assessment, monitoring and treatment of upper extremity pain in stroke patients.

Within the ICF component Activities and Participation, the ability to perform daily activities is crucial in people's lives. To measure daily activities, a number of outcome measures are available. The Utrecht Scale for Evaluation of Rehabilitation (USER)[8] and the Barthel Index[9] are two examples of frequently used measurement instruments. The USER is included in the basic set of performance indicators that were accepted as measures of effect of inpatient rehabilitation in the Netherlands since 2013[10]. The USER covers, apart from the domain Functional Independence (comprising Mobility and Self-care) also the aspects Cognitive functioning, Pain, Fatigue, and Mood.
As knowledge on the extent to which USER subscales were sensitive to changes over time and how their responsiveness compares to that of the Barthel Index, the aim of the observational

study described in **Chapter 3** was to determine the responsiveness of each subscale of the USER as compared to the Barthel Index in stroke patients who received inpatient multidisciplinary rehabilitation. In this study, the USER and the Barthel Index were administered by a nurse at admission and discharge in consecutive stroke patients admitted for inpatient rehabilitation. The Effect Size and Standardized Response Mean (SRM) were calculated as measures of responsiveness. The study included 198 patients with both admission and discharge data. Their mean age was 61.5 years (standard deviation (SD) 11.8) and 125 (63.1%) were male. At admission and discharge the mean USER subscale Functional independence scores were 43.1 (SD 18.9) and 59.3 (SD 13.8) and the mean Barthel Index scores 13.3 (SD 5.4) and 18.4 (SD 3.3), respectively. The Effect Size of the USER Functional Independence scale was 0.86 and of the Barthel Index 0.94, whereas the Effect Size of the subscales Mobility, Self-care, Cognitive functioning, Pain, Fatigue and Mood were 0.85, 0.77, 0.48, 0.19, 0.40 and 0.28, respectively. The results for the SRM were in the same range. The results of this study suggested that in inpatient rehabilitation after stroke the USER was less responsive than the Barthel Index.

With respect to the impact of stroke on participation of patients with paid employment, the study described in **Chapter 4** aimed to describe the long-term course of participation in stroke patients who were in paid employment before stroke and received multidisciplinary rehabilitation. This study included 170 working patients who were <66 years 30 months after starting rehabilitation and completed the questionnaire on paid employment at 30 months. The main outcomes in this study concerned questions on their employment status (at the start of the rehabilitation and six, 12, 18, 24 and 30 months thereafter) and the Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) (Frequency, Restrictions and Satisfaction scales, range 0-100; at six, 12 and 24 months after starting rehabilitation). These USER-P scale scores (with and without items on employment) were compared between those who did and did not report paid employment at the various time points by means of Mann-Whitney U tests. The median age of the patients was 54.2 years (IQR 11.2) and 68 (40.0%) were female. The proportions of patients reporting to be in paid employment were 84.3%, 84.2%, 75.2%, 58.4% and 50.6% at 6, 12, 18, 24 and 30 months after starting rehabilitation, respectively. In those reporting paid employment, the proportions of full sick leave decreased from 61.3% to 8.0% between six and 30 months. At 24 months, all three USER-P scale scores were statistically significantly higher in patients with paid employment than in those without ($p < 0.001$). Similar results were seen without employment items, except for the Frequency scale. The Frequency scale scores without employment items diminished over time in patients with paid employment (β -1.74, CI -2.96 – -0.52, $p = 0.005$). With respect to USER-P scale scores over time with items on employment, there were no statistically significant changes over time. In conclusion, about half of working patients had paid employment at 30 months after starting stroke rehabilitation. At 24 months, patients with paid employment experienced less restrictions and more satisfaction with participation than those without. However, without the item on employment, frequencies of participation did not differ. These results in patients with and without paid employment

might improve by implementing more consistently effective work-directed interventions and interventions for achieving meaningful participation outside of employment.

Given the substantial consequences of stroke in many patients, effective self-management skills are very important. According to the ICF, such skills could be classified under Personal Factors. Patient activation is a concept that is closely related to self-management. Patient activation was found to be related to more favourable outcomes in a number of conditions, however knowledge on patient activation and its course in stroke patients was scarce. Therefore, the study described in **Chapter 5** aimed to examine patient activation at the start of stroke rehabilitation and its course during six months follow-up. This study included 478 stroke patients who received inpatient or outpatient multidisciplinary rehabilitation and were included in the SCORE study. They had a median age of 63.0 years (IQR 56.0-70.0 years) and 308 (64.2%) were male. Patient activation was measured with the Patient Activation Measure (PAM, score 0-100, four levels, higher score and level denotes more patient activation)[11]. The PAM was measured at the start of the rehabilitation, and three and six months thereafter. At the start of the rehabilitation, the mean PAM score was 60.2 (SD 14.3), with the number of patients in PAM levels 1, 2, 3 and 4 being 76 (17.8%), 85 (19.9%), 177 (41.4%) and 90 (21.0%), respectively. Multivariate mixed model analysis demonstrated that the PAM score increased over time (start of the rehabilitation 60.2 (SD 14.3) versus three months 60.7 (SD 14.8) versus six months 61.9 (SD 18.0), $p = 0.007$). Between the start of the rehabilitation and six months, 122 (41.4%) patients remained at the same PAM level, whereas in 105 (35.6%) patients the level increased and in 68 (23.1%) patients the level decreased. At all timepoints >35% of patients had a score matching PAM levels 1 or 2. This study concluded that PAM scores increased slightly over time from the start of the rehabilitation up to six months follow-up. However, more than a third of patients had relatively low levels (i.e. levels 1 and 2) of patient activation, indicating that specific interventions during rehabilitation to increase patient activation might be of value.

Within the ICF, 'support and relationships' are an element of Environmental factors. For stroke patients, support from their immediate family is very important. This support may however also place a burden on caregivers. The study presented in **Chapter 6** aimed to describe the course of burden in individual caregivers in the first year after stroke. For that purpose, caregivers of patients included in the SCORE study were asked to complete the Caregiver Strain Index (13 items with dichotomous outcome categories (yes/no); a score of seven or more indicates a high level of burden)[12] at six and 12 months after starting rehabilitation. A total of 129 caregivers were included, of whom 19 (26.4%) were male, with a median age of 59 (range 27–78) years. Of those caregivers, 72 completed the Caregiver Strain Index twice. A consistently high or low burden was reported by 15 (20.8%) and 49 (68.1%) caregivers, respectively, whereas 8 (11.1%) reported a high burden at either six (n = 3) or 12 months (n = 5). About a third of the caregivers of stroke patients experiences a high burden, with that burden being persistent in about two-

thirds of this subgroup. As in a minority (11.1%) the caregiver burden changes from six to 12 months, it should be measured repeatedly until 12 months after stroke.

Another category of Environmental Factors are 'services, systems and policies', which includes the use of the healthcare system. However knowledge on healthcare usage in stroke patients, in particular those admitted for multidisciplinary rehabilitation, and on the longer term, is relatively scarce. When healthcare usage is studied, not only its relationship with the patients' health status and overall quality of life are relevant, but the associated costs are of interest as well. From a societal perspective, apart from healthcare costs, the costs incurred due to productivity losses must be taken into account as well. These indirect costs are directly associated with the ICF component Activities and Participation, of which work and employment are important aspects. The extent and course of participation in working stroke patients have already been addressed in **Chapter 4.** The study described in **Chapter 7** focused on both direct and indirect costs of stroke in the total population of stroke patients who received multidisciplinary rehabilitation. It aimed to estimate the societal costs and changes in health-related quality of life in stroke patients, up to one year after the start of multidisciplinary rehabilitation. Consecutive patients included in the SCORE study completed questionnaires on their health-related quality of life (EuroQol-5 Dimensions-3Levels, EQ-5D-3L)[13], absenteeism, out-of-pocket costs and healthcare use at the start and end of rehabilitation and six and 12 months thereafter. Clinical characteristics and rehabilitation costs were extracted from the medical and financial records, respectively. Data from 313 stroke patients were analysed for this cost analysis study, their mean age was 59 (SD 12) years, 185 (59.1%) were male, and 244 (78.0%) were inpatients. The mean costs for inpatient and outpatient rehabilitation were US$70,601 and US$27,473, respectively. For inpatients, health-related quality of life increased significantly between baseline and six months (EQ-5D-3L index 0.66 to 0.73, $p = 0.01$; visual analogue scale 0.77 to 0.82, $p < 0.001$) and between baseline and 12 months (EQ-5D-3L index 0.66 to 0.69, not significant; visual analogue scale 0.77 to 0.81, $p < 0.001$). It was concluded that the societal costs in the year after admission to a rehabilitation centre for stroke are considerable, yet it was also found that health-related quality of life increased significantly over time.

General Discussion

This thesis aimed to describe the long-term course of pain, participation, patient activation, caregiver burden, healthcare usage and costs in stroke patients who received multidisciplinary rehabilitation. Furthermore, it aimed to assess whether the USER or the Barthel Index can be used best to describe functional independence in stroke patients admitted for rehabilitation. At the time the studies described in this thesis were designed, the ICF[1], and in particular the ICF Core Set for Stroke[2] was the most commonly used framework capturing the complex outcomes of stroke. According to that framework, this thesis addressed a number of areas that were underrepresented in the literature so far. The knowledge gaps did not so much relate to the topics per se, but rather to a lack of insight into their extent and/or course over time, in the specific population of stroke patients who received multidisciplinary rehabilitation.

Overall it was found that the long-term consequences of stroke are substantial. These consequences do not only affect the individual stroke patient (pain, limitations in daily activities, restrictions in participation, reduced patient activation), but also affect their caregivers (caregiver burden) and healthcare and society as well (healthcare use and direct and indirect societal costs).

Methodological Considerations

Measuring outcomes in stroke care and research

In the past years, a number of frameworks or sets of instruments to measure outcomes in stroke have been published, apart from the ICF Core Set for Stroke[2]. In particular the International Consortium of Health Outcome Measurement (ICHOM) Standard Set for Stroke[3] and the Minimal Data Set Acquired Brain Injury (MDS-ABI)[4] are noteworthy. These sets recommend specific outcome measures to be used, in contrast to the ICF Core Set for Stroke, that comprises only the aspects of health that are most relevant for stroke patients[2].

In general, all of the areas addressed in this thesis (upper extremity pain, functional independence, participation in stroke patients with paid employment, patient activation, caregiver burden, and healthcare usage and costs) with the exception of costs, are included in the comprehensive ICF Core Set for Stroke[2]. However, the brief version does not include pain, paid employment or participation, or Personal factors reflecting patient activation.

The ICHOM Standard Set for stroke and the MDS-ABI lack measurements related to patient activation, caregiver burden or healthcare usage and costs, whereas the MDS-ABI does not include measures reflecting pain either[3,4]. The studies presented in this thesis underpin the relevance of all of these aspects, thereby confirming the appropriateness of the selection of most relevant aspects of stroke patients' health in the comprehensive ICF Core Set for Stroke[2].

Although the ICHOM Standard Set for Stroke and the MDS-ABI do not cover all categories or aspects relevant for stroke, the benefit of these frameworks or sets of instruments is that they recommend specific measurement instruments and thereby a uniform measuring method. Regarding the recommended instruments in the ICHOM Standard Set for stroke and MDS-ABI it must be noted that knowledge on their ability to serve as a means to monitor, evaluate and improve the quality of rehabilitation care for stroke patients is still unknown. An example is the Patient Reported Outcomes Measurement Information System (PROMIS)-10 that is included in the ICHOM Standard Set for Stroke. That instrument has so far been mainly used in hospital-based stroke populations[14]. Despite of the use of uniform outcomes measures, it should be noted that due to differences in study and patient characteristics and reference values, comparisons should be made with caution.

Apart from the optimal composition of the set of outcome measures reflecting the complex outcome of stroke, the timing of the measurements is also important. The studies presented in this thesis make it clear that in the rehabilitation population long-term follow-up is essential, because longstanding consequences of stroke are substantial and change over time for a proportion of patients. Indeed, it appeared from our studies that at 12-30 months after admission, there was a considerable proportion of patients with upper extremity pain and reduced participation and satisfaction with participation, substantial healthcare usage and of caregivers experiencing a high burden. However, in a paper on the ICHOM Standard Set for Stroke a full assessment is only recommended until 90 days after the initial event and survival is recommended to measure yearly[3]. The authors of the MDS-ABI[4] and the ICF Core Set for Stroke[2] give no recommendations on when to measure. In order to better capture the extent of the longstanding consequences of stroke (international) agreement on both the content of a comprehensive set of outcome measures and the recommended frequency of its administration on the longer term is needed.

Strengths and limitations of the SCORE study

A prospective cohort study including consecutive patients with stroke admitted for rehabilitation is ideal to study the long-term outcomes in this specific patient group. A strength of the SCORE study concerns its sample size, because, as compared to other cohort studies, it comprises a relatively large number of stroke patients (901 by 2021). Moreover, as it only includes patients who receive multidisciplinary inpatient or outpatient rehabilitation, it gives a profound insight into the outcomes and their course in this specific subgroup of stroke patients. The follow-up duration of 30 months after the start of the rehabilitation provides insight into the course of several outcome measures on the long-term. This is important from the clinical point of view, as the duration of routine follow-up is usually limited, so that rehabilitation professionals are generally unaware of the eventual outcomes of their treatment. This includes also the possible occurrence of new problems or aggravating of persisting ones, constituting a possible

renewed indication for consultation of a rehabilitation physician. Another strength concerns the broad range of outcome measures employed, including relatively under-studied areas such as pain, patient activation or costs.

The setup of a large prospective cohort study enables the conduct of embedded studies evaluating the effectiveness of interventions. An example of such studies are those with a pre-test post-test design, where outcomes are compared between patients admitted in a period where an intervention was not used and a period where it was implemented. This methodology was used in the Fit After Stroke (FAST)@Home study, evaluating the effectiveness of an integrated eHealth platform by efficiently making use of data gathered in the context of the ongoing SCORE study[15].

Although more knowledge about the subgroup of stroke patients who received multidisciplinary rehabilitation is valuable, it can also be seen as a limitation. Extending the cohort study to all patients with stroke could yield valuable insights into differences and similarities of outcomes of patients discharged to their homes or admitted for geriatric rehabilitation. For that purpose, the SCORE+ Study was developed, that included patients from September 2020 to September 2021 in the Haaglanden Medical Centre (led by HJ Arwert, K Jellema, SJ Tamminga and TPM Vliet Vlieland) and included 342 patients.

Another limitation concerning the selection of patients is that patients with severe aphasia and severely affected patients were not able to participate, as they could not complete questionnaires. Moreover, the treating physicians needed to personally invite patients for the study, which leaded to more administrative tasks for them and therefore some eligible patients might be missed. Another form of selection occurred with the analyses, that were in some of the studies in this thesis performed within a subgroup of patients, namely those who completed the follow-up. It was found in a number of analyses that the patients completing the measurements differed from those who did not with respect to living alone, having a prior myocardial infarction, alcohol consumption, higher level of frailty and education level[7,16].

Another drawback of the study concerns the intervention. Overall, multidisciplinary inpatient or outpatient rehabilitation is, despite the availability of guidelines[17,18], overall not very much standardized and in part not sufficiently recorded on the individual patient level. A previous comparison of the structure (four centres)[6] and processes (two centres)[19] of stroke rehabilitation indeed found significant differences. For the structure of rehabilitation these concerned aspects such as admission and discharge criteria, the presence and content of patient subgroups, the presence and duration of care pathways, the timing of team meetings, the timing of clinical assessments, the maximum time from hospital discharge to admission, the content of aftercare and return to work modules, the types of medical and paramedical treatment disciplines, the types of facilities for treatment and diagnosis, and the content

of strategies for caregiver involvement[6]. Regarding the process of care, differences were seen with respect to the number of hours of speech and language therapy, psychology and recreational therapy. However it appeared that overall the outcomes were in general similar[19].

Finally, the downside of the wealth of data concerns the burden for patients to complete all the questionnaires and questions at multiple time points. This is a considerable drawback, in particular as the data were gathered alongside of clinical care and were not used by clinicians and patients to set and evaluate treatment goals.

Patient Research Partners

Besides the above mentioned strengths of the SCORE study, there is another one, worth mentioning separately: the involvement of patient research partners. In order to ensure that the design of the SCORE study, including the research questions, were relevant to stroke patients and their caregivers, a panel of patient research partners was set up from the beginning of the study[20]. Patient participation in research is important, because the views of all those with legitimate interests should be included and it increases the social impact of research[21,22].

The panel of research partners of the SCORE study comprised about eight patients and one caregiver. These patients suffered from stroke or acquired brain injury, received inpatient and/or outpatient rehabilitation at Basalt and were motivated to share their perspective and thereby improving research. In the period 2013 until present the research partners met with the investigators once or twice per year. During the meetings long-term changes and needs after stroke and return to work were mentioned, which resulted in an amendment and article, respectively. The research partners also played a role in preparing the invitation and programme of the SCORE day in 2019 held in Leiden and the Hague. The SCORE day was organised in honour of the fifth anniversary of the SCORE study and at this day all participants of the study were informed about the results of the SCORE study. Ninety patients and their partners attended the SCORE day in Leiden and 123 in the Hague and they appreciated sharing experiences with fellow patients and partners.

Due to the valuable contribution of the research partners to the SCORE study, this concept has been extended within Basalt to other studies and the formation of a new panel: patient innovation partners. The patient innovation partners are giving their input on eHealth innovations and its implementation in rehabilitation care. They are involved in composing plans on eHealth, in helping to develop and test innovations and in giving critical advices. This involvement will ensure more successful implementation of eHealth in rehabilitation care.

Measurement instruments

To adequately measure the outcome of interest, a measurement instrument should have adequate measurement properties[23]. It must be noted that for a number of instruments that are recommended in the ICHOM Standard Set for Stroke and the MDS-ABI not all measurement properties, interpretability and cut-off values in a stroke rehabilitation population are known. For example, concerning content validity, criterion validity and cross cultural validity/ measurement invariance in stroke populations of the PROMIS Global Health no studies were found[24].

To evaluate treatment, responsiveness, i.e. the ability to capture improvement or deterioration of a patient's health status is an important measurement property[23]. In this thesis, the responsiveness of the USER was evaluated, by computing its effect size (ES) and standardized response mean (SRM) between admission and discharge of stroke patients in rehabilitation and comparing these with those of the Barthel Index. Although with ES and SRM some insight into responsiveness can be obtained, it must be noted that the most adequate methodology to evaluate an instrument's responsiveness should include an assessment of longitudinal validity. In analogy to construct validity, longitudinal validity should be assessed by testing predefined hypotheses, e.g., about expected correlations between changes in measures, or expected differences in changes between "known" groups[23]. A weakness of this methodology concerns the formulation of hypotheses, where the expectations of the strength of the correlations may vary among researchers. Since our study did not use an assessment of longitudinal validity, the conclusions must be interpreted with some caution.

A challenge regarding the optimal composition of the set of outcome measurements, is the potential tension among the major objectives of the measurements: for individual patient care or for quality of care purposes, within or across institutions. For a number of generic instruments, relevant measurement properties in specific patient groups have been insufficiently established, with the uncertain suitability of the PAM in stroke patients admitted for rehabilitation (**Chapter 5**) as an example. In general, for many instruments the cut-off values to distinguish individual patients with different levels of health problems and healthcare needs are absent, so that their usability in individual patient care is limited. A specific drawback of generic measurement instruments is that they might not be applicable in patients with a specific condition such as stroke.

Implications for research

Overall the SCORE study showed that in stroke patients admitted for inpatient or outpatient rehabilitation long-term assessments consisting of a comprehensive set of outcome measures are feasible and provide valuable insights[7].

Given the abovementioned strengths and limitations of the SCORE study, a number of recommendations for the continuation of this study can be made, which could also be applicable to other observational cohort studies:

1) The recruitment process can be facilitated by decreasing administrative activities for the treating physicians needed to invite patients for the study; in this way the missing of patients for logistic reasons can be diminished; 2) The set of questionnaires should in general be limited and simplified so that the willingness to participate and compliance will increase; 3) The optimal composition of the set of measurement instruments can be reconsidered, based on the instruments advised in the ICHOM Standard Set for Stroke and/or MDS-ABI. In this respect, currently recommendations on outcome measures in stroke care in the Netherlands are developed as part of the national program Uitkomstgerichte Zorg[25] and should be taken into account. Moreover, from an international perspective there are initiatives to monitor the quality of rehabilitative care by assessing the responsiveness of newly developed quality indicators for rehabilitation[26]; 4) The use of CAT versions of questionnaires could be considered, to limit the number of questions to be answered; Such formats are available for a number of PROMIS instruments; 5) As communication problems are common in stroke patients, the inclusion of clinical tests could be considered, but that would require adequate resources for the time and other expenses associated with the execution of such tests. Another option would be the use of questionnaires which can be filled in by all patients despite communication problems. Such using digital technology are currently being developed[27].

Besides selecting the appropriate measurement instruments other challenges regarding research in a stroke rehabilitation population are present. For rehabilitation in general, the evidence for specific interventions, either or not consisting of single or multiple treatment modalities delivered by one or more professions, is scanty. For example, this thesis found that patient activation was low in stroke patients who reived rehabilitation[28]. However, we do not know yet which interventions are successful for this group. In stroke rehabilitation in particular, the presence of practice variation was indeed suggested[6,19], a finding that may point into the possibility of suboptimal care delivery. More research into the cost-effectiveness of multidisciplinary rehabilitation interventions is needed to unravel the "black box", e.g. by comparing the outcomes (effectiveness, costs and satisfaction of patients and healthcare providers) of different care pathways for patients with specific patterns of problems and limitations.

The availability of an ongoing cohort study at multiple locations may facilitate the conduct of such research, as this enables the execution of pre-test post-test studies as well as nested randomized controlled trials. However, for the execution of these types of studies it is important that the delivery of the interventions is accurately registered at patient level. This registration needs improvement.

Implications for clinical practice

Assessments during rehabilitation

The results of studies presented in this thesis suggest that in stroke patients who receive multidisciplinary rehabilitation more attention is needed for diagnosis and treatment of upper extremity pain, other means of meaningful participation in case return to paid employment seems unattainable, and increasing patient activation as a prerequisite for effective self-management[28]. In addition, it was also found that a considerable proportion of caregivers experiences a large burden[29].

This enhanced attention should not be limited to the recognition of these problems, but to the institution of adequate interventions as well. It is conceivable that the subacute phase is not the optimal timing for some of these interventions. In that case, an appropriate report to healthcare providers in outpatient rehabilitation or primary care is of utmost importance. By incorporating the abovementioned topics in routine work flows, e.g. in designated care pathways, the awareness of the importance of these elements will increase. The addition of patient-reported outcome measures in routine work flows could aid in identifying topics where support is needed.

Follow-up after rehabilitation

With respect to clinical practice, currently, in the Netherlands, follow-up after discharge from multidisciplinary rehabilitation is usually temporarily (until 6-12 months) whereas the results of this thesis suggests that on the long-term new limitations might arise. For example some restrictions in participation may only become clear on the longer term, such as permanent work disability, which is only final after two years of sick leave in many patients. Furthermore, this thesis showed that pain and caregiver burden can arise on the long-term[29]. Improvements could consist of the implementation of a standardized system of surveillance, to identify patients at risk for deterioration. As it appeared that long-term healthcare usage in primary care was substantial, the setup of a surveillance system could well be done in close collaboration with e.g. general practitioners, specialized stroke nurses working in the community and physical therapists[30]. Furthermore, general practitioners and stroke nurses should know to which paramedics and rehabilitation physicians they can refer stroke patients. In the region Zuid-Holland occupational therapists, physical therapists and speech and language therapist in primary care with experience with patients with neurological complaints are gathered in a network (Neuronet) in order to secure and possibly improve care for patients with neurological complaints[31].

Overall, this thesis filled some knowledge gaps on long-term outcomes after stroke rehabilitation. However, many challenges remain regarding research and clinical practice.

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Chapter 9

Nederlandse samenvatting

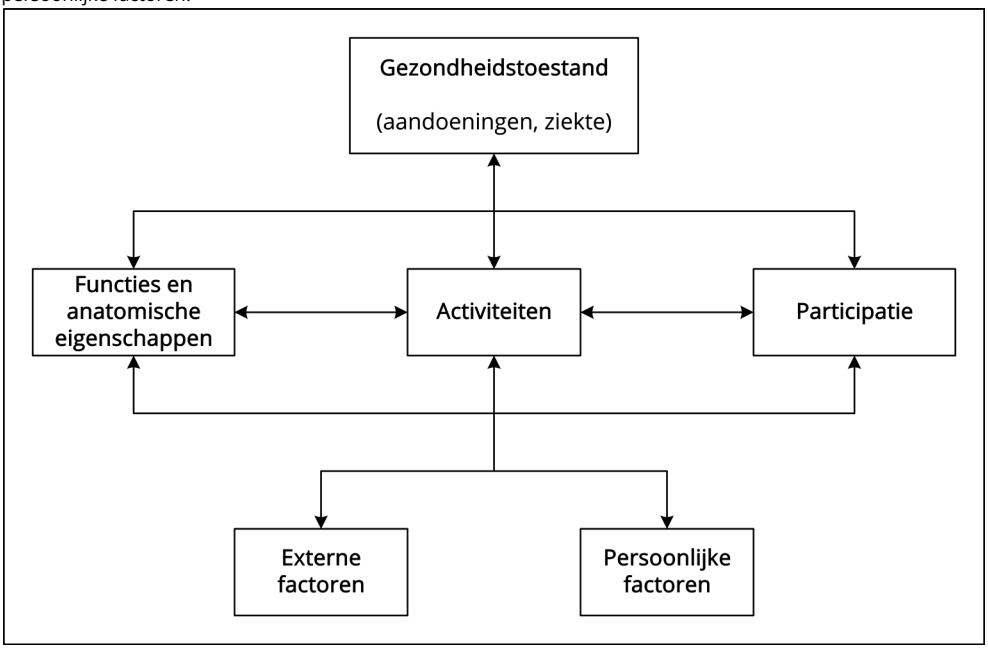
Samenvatting

Een beroerte, of cerebrovasculair accident (CVA), is een veel voorkomende aandoening die wordt veroorzaakt door een blokkade van een bloedvat (infarct) of scheuring van een bloedvat (bloeding) in de hersenen[1]. Ondanks dat de acute behandeling is verbeterd, heeft een beroerte bij veel patiënten een blijvende invloed op hun dagelijks leven. Een beroerte kan namelijk leiden tot beperkingen op het gebied van het lichamelijk, cognitief, emotioneel, communicatief, sociaal en/of maatschappelijk functioneren. De gevolgen van een beroerte zijn daarmee niet alleen groot voor de patiënten zelf en hun naasten, maar ook voor de gezondheidszorg en de samenleving in het algemeen.

Om de verscheidenheid aan gevolgen na een beroerte systematisch te kunnen beschrijven, is een kader nodig. De 'International Classification of Functioning, Disability and Health' (ICF) van de Wereldgezondheidsorganisatie (WHO) is een voorbeeld van een dergelijk kader[2,3] (figuur 1). De ICF biedt gestandaardiseerde begrippen om gezondheidsuitkomsten te beschrijven op het gebied van functies en anatomische eigenschappen, activiteiten en participatie. De ICF bestaat uit de componenten '*functies en anatomische eigenschappen*', '*activiteiten en participatie*' en *'contextuele factoren' (omgevingsfactoren en persoonlijke factoren)*[2]. Specifiek voor beroerte werden de ICF Core Sets voor beroerte ontwikkeld[3]. Deze Core Sets bevatten díe specifieke aspecten van de gezondheid die het meest relevant zijn voor patiënten met een beroerte[3]. Andere sets om de gevolgen van een beroerte systematisch te beschrijven zijn bijvoorbeeld de zogenaamde Standard Set for Stroke van het International Consortium of Health Outcome Measurement (ICHOM)[4] en de Minimal Data Set niet aangeboren hersenletsel (MDS-ABI)[5]. Deze laatste twee sets omvatten specifieke meetinstrumenten, die inhoudelijk grotendeels overeenkomen met de gezondheidsaspecten binnen de ICF Core Sets voor beroerte.

Hoewel er veel onderzoek is gedaan naar de gevolgen van een beroerte, zijn er nog steeds kennislacunes. Dit proefschrift behandelt zes van deze kennislacunes, waarbij een subgroep van patiënten met een beroerte onderzocht is: patiënten die gebruik maakten van multidisciplinaire revalidatie. Bovendien richt dit proefschrift zich niet alleen op de subacute (revalidatie) fase, maar ook op de chronische fase tot 30 maanden na de beroerte.

Figuur 1. het ICF Model: de wisselwerking tussen de verschillende aspecten van de gezondheid en externe en persoonlijke factoren.



Dit proefschrift bevat, met uitzondering van één hoofdstuk (**hoofdstuk 3**), gegevens van de Stroke Cohort Outcomes of REhabilitation (SCORE)-studie. Deze studie is opgezet en uitgevoerd in twee revalidatiecentra: het Rijnlands Revalidatie Centrum in Leiden en Sophia Revalidatie in Den Haag (inmiddels zijn deze revalidatiecentra gefuseerd tot Basalt)[6-8]. In deze studie werden tussen 2014 en 2019 alle opeenvolgende patiënten met een beroerte die gebruik maakten van multidisciplinaire klinische of poliklinische revalidatie geïncludeerd. Vanaf de start van de revalidatie tot 30 maanden daarna werden er metingen uitgevoerd.

De onderzoeksvragen van de SCORE-studie waren (**hoofdstuk 1**):
1) het beschrijven van de functies, activiteiten, participatie en kwaliteit van leven van patiënten met een beroerte, op de korte en lange termijn;
2) het beschrijven van aan de beroerte gerelateerde kosten vanuit het perspectief van een revalidatiecentrum, de gezondheidszorg en de samenleving.

Dit proefschrift behandelt beide bovengenoemde overkoepelende onderzoeksvragen, waarbij alle drie de componenten van de ICF aan bod komen, d.w.z. pijn in de bovenste extremiteit (*functies en anatomische eigenschappen*), zelfstandigheid bij activiteiten van het dagelijks leven en betaald werk (*activiteiten en participatie*), patiënt activatie (contextuele factoren: *persoonlijke factoren*), mantelzorgerlast en zorggebruik en kosten (contextuele factoren: *externe factoren*).

De algemene doelstellingen van dit proefschrift zijn:

- beschrijven van het lange termijn verloop van pijn, participatie, patiënt activatie, mantelzorgerlast, zorggebruik en kosten en;
- nagaan of de Utrechtse Schaal voor Evaluatie van Revalidatie (USER) of de Barthel Index het best gebruikt kan worden voor het beschrijven van de functionele zelfstandigheid bij patiënten met een beroerte die klinisch revalideren.

Op het niveau van de ICF component *'functies en anatomische eigenschappen'* was het doel van de studie beschreven in **hoofdstuk 2** om het verloop van de aanwezigheid en de intensiteit van pijn in de schouder, arm, pols of hand bij patiënten met een beroerte te beschrijven. In totaal namen 678 patiënten met een beroerte die gebruik maakten van multidisciplinaire revalidatie deel aan deze studie. Drie, 18 en 30 maanden na de start van de revalidatie vulden zij een vraag in over de aanwezigheid van pijn in de schouder, arm, pols, of hand (ja/nee). Indien aanwezig, beoordeelden zij de ernst van de pijn op een visuele analoge schaal (VAS) van 0 (d.w.z. helemaal geen pijn) tot 10 (d.w.z. de ergst denkbare pijn). Vervolgens werden het aantal patiënten met pijn en de intensiteit van de pijn over de tijd in kaart gebracht.
De aantallen patiënten die pijn in de bovenste extremiteit rapporteerden waren 260/622 (42%) na 3 maanden, 187/519 (36%) na 18 maanden en 146/446 (33%) na 30 maanden. Deze afname van het percentage patiënten dat pijn rapporteerde in de loop van de tijd was statistisch significant ($p < 0.001$). Bij patiënten die pijn in de schouder, arm, pols, of hand rapporteerden, was de mediane ernst van de pijn 5.0 (interkwartielafstand, interquartile range (IQR) 3.0) na drie en 18 maanden en 5.0 (IQR 4.0) na 30 maanden. Bij de 73 patiënten die op alle tijdstippen pijn rapporteerden, was de mediane score voor de ernst van de pijn 6.0 (IQR 2.5) na drie maanden, 5.0 (IQR 3.0) na 18 maanden en 5.0 (IQR 3.0) na 30 maanden. Deze afname over de tijd was niet significant ($p = 0.06$).
De conclusie van het onderzoek was dat het aantal patiënten met pijn in de schouder, arm, pols, of hand na een beroerte aanzienlijk is, hoewel hun aantal over een periode van 2.5 jaar wel afnam van 42% naar 33%. Bij de patiënten die pijn rapporteerden, leek de ernst van de pijn in de loop van de tijd niet af te nemen. Deze resultaten suggereren dat er ruimte is voor verbetering van de beoordeling, monitoring en behandeling van pijn in de bovenste extremiteit bij patiënten met een beroerte.

Binnen de ICF component *'activiteiten en participatie'* is het zelfstandig kunnen uitvoeren van dagelijkse activiteiten van cruciaal belang in het leven van mensen. Er is een aantal meetinstrumenten beschikbaar om deze zelfstandigheid bij het doen van dagelijkse activiteiten te meten. Twee voorbeelden van veelgebruikte meetinstrumenten zijn de Utrechtse Schaal voor Evaluatie van Revalidatie (USER)[9] en de Barthel Index[10]. De USER bevat naast de subschaal lichamelijk functioneren (bestaande uit mobiliteit en zelfverzorging) ook de subschalen cognitief functioneren, pijn, vermoeidheid en stemming.

Om resultaten van een behandeling goed te kunnen meten, is het belangrijk om te weten in hoeverre de USER subschalen en de Barthel Index gevoelig zijn voor veranderingen over de tijd (responsiviteit). Het doel van de observationele studie beschreven in **hoofdstuk 3** was daarom om de responsiviteit van de subschalen van de USER te bepalen en te vergelijken met de responsiviteit van de Barthel Index bij patiënten met een beroerte die klinisch revalideerden. Beide meetinstrumenten werden bij opname en ontslag door een verpleegkundige afgenomen. Als maat voor responsiviteit werden de effectgrootte (Effect Size, ES) en het gestandaardiseerde responsgemiddelde (Standardized Response Mean, SRM) van de USER en de Barthel Index berekend.
Van 198 patiënten waren zowel opname- als ontslaggegevens bekend. Hun gemiddelde leeftijd was 61.5 jaar (standaarddeviatie (SD) 11.8) en 125 (63.1%) van de patiënten was man. Bij opname en ontslag waren de gemiddelde scores van de USER subschaal lichamelijk functioneren respectievelijk 43.1 (SD 18.9) en 59.3 (SD 13.8) en de gemiddelde scores van de Barthel Index 13.3 (SD 5.4) en 18.4 (SD 3.3). De ES van de USER lichamelijk functioneren (0.86) en van de Barthel Index (0.94) waren hoog. De ES van de USER subschalen mobiliteit, zelfverzorging, cognitief functioneren, pijn, vermoeidheid en stemmingen waren respectievelijk 0.85, 0.77, 0.48, 0.19, 0.40 en 0.28. De resultaten van de SRM waren vergelijkbaar. Op basis van deze resultaten werd geconcludeerd dat de Barthel Index gevoeliger is dan de USER om veranderingen in zelfstandigheid bij het doen van dagelijkse activiteiten bij patiënten die klinisch revalideerden na een beroerte te meten.

Het doel van de studie beschreven in **hoofdstuk 4** was om het lange termijn verloop van participatie te beschrijven bij patiënten met een beroerte die gebruik maakten van multidisciplinaire revalidatie en die betaald werk hadden voor de beroerte. In deze studie zijn 170 werkende patiënten geïncludeerd die 30 maanden na de start van de revalidatie jonger dan 66 jaar waren en die na 30 maanden een vragenlijst over betaald werk invulden. De belangrijkste uitkomsten van deze studie betroffen de arbeidsstatus bij de start van de revalidatie tot 30 maanden daarna en de Utrechtse Schaal voor Evaluatie van Revalidatie-Participatie (USER-P) (frequentie, beperkingen en tevredenheid schalen, range 0-100; op 6, 12 en 24 maanden na de start van de revalidatie). De USER-P schaalscores (met en zonder items over werk) werden vergeleken tussen patiënten die wel en die geen betaald werk rapporteerden op de verschillende follow-up tijdstippen.
De mediane leeftijd van de patiënten was 54.2 jaar (IQR 11.2) en 68 (40.0%) waren vrouw. De percentages patiënten met betaald werk waren 84%, 84%, 75%, 58% en 51% op respectievelijk 6, 12, 18, 24 en 30 maanden na de start van de revalidatie. Over de tijd waren er in de schaalscores van de USER-P met items over werk geen statistisch significante veranderingen. Na 24 maanden waren alle drie de schaalscores van de USER-P met items over werk statistisch significant hoger bij patiënten met betaald werk dan zonder betaald werk ($p < 0.001$).
Zonder de items over werk waren er eveneens over de tijd in de schaalscores beperkingen en tevredenheid van de USER-P geen statistisch significante veranderingen. *Zonder* de items

over werk namen de scores van de frequentieschaal in de loop van de tijd af bij patiënten met betaald werk (p =0.005) en bleven gelijk bij patiënten zonder betaald werk. Na 24 maanden was er geen verschil in de frequentie van activiteiten anders dan werk tussen patiënten met en zonder betaald werk.
Uit deze resultaten werd geconcludeerd dat ongeveer de helft van de patiënten die betaald werk hadden voor hun beroerte, 30 maanden na de start van de revalidatie betaald werk had. Na 24 maanden ervaarde deze groep werkenden minder beperkingen in participatie en waren hierover meer tevreden dan patiënten die geen betaald werk meer hadden, ondanks dat de frequentie van activiteiten anders dan werk niet verschillend was. Deze resultaten suggereren dat er mogelijkheden zijn voor verbetering van het zorgaanbod, bijvoorbeeld door het implementeren van effectieve arbeidsgerichte interventies zodat meer voorheen werkende mensen met een beroerte betaald werk kunnen behouden. Daarnaast moet er ook aandacht zijn voor interventies om betekenisvolle mate van participatie te verkrijgen als betaald werken niet meer mogelijk blijkt.

Bij het omgaan met de gevolgen van een beroerte zijn zelfmanagementvaardigheden van groot belang. Zulke vaardigheden kunnen volgens de ICF worden ingedeeld onder *'persoonlijke factoren'*. Een concept dat nauw verwant is aan zelfmanagement is patiënt activatie. Patiënt activatie wordt gedefinieerd als: *'iemands rol in het zorgproces en het hebben van kennis, vaardigheden en zelfvertrouwen om gezondheid en gezondheidszorg te managen'*[11]. Betere patiënt activatie bleek eerder gerelateerd te zijn aan gunstigere uitkomsten voor een aantal aandoeningen, maar kennis over patiënt activatie en het verloop ervan bij patiënten met een beroerte is schaars. Het doel van de studie beschreven in **hoofdstuk 5** was daarom om bij deze groep patiënt activatie te onderzoeken bij de start van de revalidatie en het beloop ervan in de zes maanden daarna. In deze studie zijn 478 patiënten met een beroerte die klinisch of poliklinisch revalideerden geïncludeerd. De mediane leeftijd van de patiënten was 63.0 jaar (IQR 56.0-70.0 jaar) en 308 (64.2%) waren man. Patiënt activatie werd gemeten met de Patient Activation Measure (PAM, score 0-100, vier niveaus, hogere score en niveau duiden op meer activering van de patiënt)[11]. De PAM werd ingevuld bij de start van de revalidatie en drie en zes maanden daarna. Bij de start van de revalidatie was de gemiddelde PAM score 60.2 (SD 14.3) en het aantal patiënten met respectievelijk PAM niveaus 1, 2, 3 en 4 was 76 (17.8%), 85 (19.9%), 177 (41.4%) en 90 (21.0%). De gemiddelde PAM score nam enigszins toe in de loop van de tijd (tot 60.7 (SD 14.8) na drie maanden en 61.9 (SD 18.0) na zes maanden, p = 0.007). Tussen de start van de revalidatie en zes maanden daarna bleven 122 (41.4%) patiënten op hetzelfde PAM niveau, terwijl 105 (35.6%) patiënten omhoog gingen en 68 (23.1%) daalden in niveau. Meer dan 35% van de patiënten had op alle tijdstippen een score die overeen kwam met PAM niveau 1 of 2.
De conclusie van deze studie was dat de mate van patiënt activatie op groepsniveau heel licht steeg vanaf de start van de revalidatie tot 6 maanden daarna. Meer dan een derde van de patiënten had echter een laag niveau van patiënt activatie (d.w.z. niveau 1 en 2) vanaf de

start van de revalidatie tot 6 maanden daarna. Deze bevindingen duiden erop dat specifieke interventies om patiënt activatie te verhogen tijdens de revalidatie van meerwaarde zouden kunnen zijn.

Binnen de ICF vormen *'ondersteuning en relaties'* een element van *'externe factoren'*. Voor patiënten met een beroerte is de steun van hun naaste familie, vrienden en kennissen zeer belangrijk. Voor de naasten kan deze mantelzorg echter ook een belasting vormen. Het doel van de studie die wordt gepresenteerd in **hoofdstuk 6** was om het verloop van de belasting van de individuele mantelzorger in het eerste jaar na de beroerte te beschrijven. Mantelzorgers van patiënten die deelnamen aan de SCORE-studie vulden de Caregiver Strain Index (een vragenlijst met 13 ja/nee vragen; een score van zeven of meer duidt op een hoge mate van mantelzorgbelasting)[12] in op 6 en 12 maanden na de start van de revalidatie. In totaal namen 129 mantelzorgers deel aan dit onderzoek. De mediane leeftijd was 59 (range 27-78) jaar en 19 van hen (26.4%) waren mannen. Van de mantelzorgers vulden 72 de Caregiver Strain Index twee keer in. Een constante (op alle tijdstippen dezelfde) hoge of lage belasting werd gerapporteerd door respectievelijk 15 (20.8%) en 49 (68.1%) mantelzorgers, terwijl 8 (11.1%) mantelzorgers alleen na zes (n = 3) of 12 maanden (n = 5) een hoge belasting rapporteerden. Uit de resultaten van het onderzoek werd geconcludeerd dat ongeveer een derde van de mantelzorgers van patiënten met een beroerte op enig moment een hoge belasting ervaart, waarbij de belasting constant aanwezig is bij ongeveer twee derde van deze subgroep. Aangezien de hoge mantelzorgerbelasting bij 11.1% van de mantelzorgers later ontstaat, is het aan te bevelen om deze dus herhaaldelijk te meten tot 12 maanden na de beroerte.

Een andere categorie van de ICF component *'externe factoren'* is *'diensten, systemen en beleid'*. Hier valt het gebruik van gezondheidszorg onder. De kennis over zorggebruik van patiënten met een beroerte is relatief schaars, vooral over het zorggebruik van patiënten die gebruikmaken van multidisciplinaire revalidatie en op de langere termijn. Bij het in kaart brengen van zorggebruik zijn niet alleen de relatie met de gezondheid van de patiënt en de algehele kwaliteit van leven relevant, maar zijn ook de kosten van het zorggebruik van belang. Vanuit maatschappelijk perspectief moet bij het inventariseren van kosten van zorggebruik niet alleen rekening gehouden worden met de kosten van de gezondheidszorg, maar ook met de kosten als gevolg van productiviteitsverlies. Deze indirecte kosten hangen samen met de ICF component *'activiteiten en participatie'*, waar *'beroep en werk*' onderdelen van zijn. De mate en het verloop van participatie bij werkende patiënten met een beroerte zijn al aan de orde gekomen in **hoofdstuk 4**. De studie beschreven in **hoofdstuk 7** richtte zich op de directe en indirecte kosten van een beroerte bij patiënten die gebruik maakten van multidisciplinaire revalidatie. Het doel was om een schatting te maken van de maatschappelijk kosten en van veranderingen in de gezondheid gerelateerde kwaliteit van leven van patiënten met een beroerte vanaf de start van de revalidatie tot 12 maanden daarna. Patiënten die deelnamen aan de SCORE-studie vulden vragenlijsten in over hun gezondheid gerelateerde kwaliteit van leven

(EuroQol 5-Dimensions 3-Levels, EQ-5D-3L), ziekteverzuim, met de beroerte samenhangende kosten die zij uit eigen zak moesten betalen en het zorggebruik, bij de start en aan het eind van de revalidatie en zes en 12 maanden daarna. Kenmerken van de beroerte en kosten van de revalidatie werden respectievelijk uit de medische dossiers en de financiële registraties van het revalidatiecentrum gehaald.
Voor deze kostenanalyse werden gegevens van 313 patiënten met een beroerte geanalyseerd. Hun gemiddelde leeftijd was 59 (SD 12) jaar, 185 (59.1%) waren man en 244 (78.0%) van de patiënten ontving klinische revalidatie. De gemiddelde totale kosten per patiënt vanaf de start van de klinische of poliklinische revalidatie tot 12 maanden daarna bedroegen respectievelijk US$70.601 (€63.045) en US$27.473 (€24.533). Bij klinische patiënten nam de gezondheid gerateerde kwaliteit van leven significant toe tussen de start van de revalidatie en zes maanden (EQ-5D-3L index 0.66 tot 0.73, p = 0.01; visuele analoge schaal 0.77 tot 0.82, p < 0.001) en tussen de start van de revalidatie en 12 maanden (EQ-5D-3L index 0.66 tot 0.69, niet significant; visuele analoge schaal 0.77 tot 0.81, p < 0.001). Er werd geconcludeerd dat de maatschappelijke kosten van een beroerte in het eerste jaar van revaliderende patiënten aanzienlijk zijn, maar ook dat de gezondheid gerelateerde kwaliteit van leven toenam over de tijd.

Discussie

Het doel van dit proefschrift was om het lange termijn verloop van pijn, participatie, patiënt activatie, mantelzorgerlast, zorggebruik en kosten te beschrijven bij patiënten met een beroerte die gebruik maakten van multidisciplinaire revalidatie. Daarnaast was het doel om na te gaan welk meetinstrument in deze patiëntengroep het beste gebruikt kan worden om zelfstandigheid bij het doen van dagelijkse activiteiten te beschrijven: de USER of de Barthel Index. Ten tijde van het ontwerpen van de studies die in dit proefschrift zijn beschreven, werd de ICF[2], en in het bijzonder de ICF Core Set voor beroerte[3], het meest gebruikt om de complexe uitkomsten na een beroerte vast te leggen. Dit proefschrift richtte zich op zes kennislacunes betreffende verschillende onderdelen van de gezondheid in verschillende componenten van de ICF. De kennislacunes hadden niet zozeer betrekking op de onderwerpen op zich, maar op een gebrek aan inzicht in de omvang en/of het verloop op langere termijn in de specifieke populatie van patiënten met een beroerte die gebruik maakten van multidisciplinaire revalidatie.

In het algemeen werd vastgesteld dat de gevolgen van een beroerte ook op de lange termijn aanzienlijk zijn. Deze gevolgen hebben niet alleen invloed op de individuele patiënt (pijn, beperkingen in activiteiten van het dagelijks leven, beperkingen in participatie), maar ook op hun naasten (mantelzorgerlast) en de gezondheidszorg en samenleving (zorggebruik en directe en indirecte maatschappelijke kosten).

Methodologische overwegingen

Het meten van uitkomsten bij patiënten met een beroerte in zorg en onderzoek

In de afgelopen jaren zijn, naast de ICF Core Sets voor beroerte[3], een aantal uitkomstensets gepubliceerd om de gevolgen van een beroerte gestandaardiseerd in kaart te brengen. De zogenaamde Standard Set for Stroke van het International Consortium of Health Outcome Measurement (ICHOM)[4] en de Minimal Data Set niet aangeboren hersenletsel (MDS-ABI)[5] bevelen specifieke meetinstrumenten aan. De ICF Core Sets voor beroerte duiden vooral aan welke aspecten van de gezondheid relevant zijn, zonder aan te geven welke meetinstrumenten daarvoor gebruikt moeten worden[3].

Alle onderwerpen die in dit proefschrift aan de orde komen zijn, met uitzondering van de kosten, onderdeel van de uitgebreide ICF Core Set voor beroerte[3]. In de beknopte ICF Core Set voor beroerte ontbreken echter pijn, betaald werk of participatie of persoonlijke factoren die de patiënt activatie weerspiegelen.

De ICHOM Standard Set for Stroke en de MDS-ABI bestrijken niet alle categorieën of aspecten die relevant zijn voor beroerte: in de ICHOM Standard Set for Stroke en de MDS-ABI ontbreken meetinstrumenten met betrekking tot patiënt activatie, mantelzorgerlast en gebruik en kosten van gezondheidszorg[4,5]. De MDS-ABI bevat ook geen meetinstrument dat pijn weerspiegelt[5]. De studies die in dit proefschrift gepresenteerd worden, onderbouwen de relevantie van al deze aspecten. Daarmee bevestigen ze de juistheid van de selectie van de meest relevante aspecten van gezondheid van patiënten met een beroerte in de uitgebreidere ICF Core Set voor beroerte[3].

Het voordeel van de ICHOM Standard Set for Stroke en de MDS-ABI is wel dat zij specifieke meetinstrumenten aanbevelen en daarmee een uniforme meetmethode. Echter, de kennis over het vermogen van veel van de aanbevolen meetinstrumenten om de kwaliteit van de revalidatiezorg voor patiënten met een beroerte te monitoren, te evalueren en te verbeteren op het individuele patiëntniveau is nog onbekend. Een voorbeeld is het Patient Reported Outcomes Measurement Information System (PROMIS-10) dat is opgenomen in de ICHOM Standard Set for Stroke. Tot nu toe is dat instrument voornamelijk gebruikt bij patiënten met een beroerte die zijn opgenomen in het ziekenhuis[13].

Naast de optimale samenstelling van de set van uitkomstmaten die de complexe gevolgen van een beroerte weerspiegelen, is ook de timing van de metingen van belang. De studies die in dit proefschrift gepresenteerd worden, maken duidelijk dat langdurige follow-up essentieel is in een revalidatiepopulatie. De langdurige gevolgen van een beroerte zijn namelijk aanzienlijk en voor een deel van de patiënten veranderen deze in de loop van de tijd. Uit de studies in dit proefschrift bleek dat er 12-30 maanden na de start van de revalidatie een aanzienlijk deel

patiënten was met pijn in de bovenste extremiteit, verminderde participatie en tevredenheid met participatie, substantieel zorggebruik en dat er mantelzorgers waren die een hoge belasting ervoeren. In een artikel over de ICHOM standaard set voor beroerte wordt echter een volledige beoordeling aanbevolen tot slechts 90 dagen na de beroerte en of patiënten in leven zijn wordt aanbevolen om jaarlijks te meten[4]. De auteurs van de MDS-ABI[5] en de ICF Core Set voor beroerte[3] geven geen aanbevelingen over het meetmoment. Om de omvang van de langdurige gevolgen van een beroerte beter in kaart te brengen is (internationale) overeenstemming nodig over zowel de samenstelling van een uitgebreide set uitkomstmaten als de aanbevolen frequentie van de afname daarvan op de langere termijn. Tot slot moet worden opgemerkt dat ook bij het gebruik van uniforme uitkomstmaten vergelijkingen tussen de uitkomsten van verschillende patiëntenpopulaties met de nodige voorzichtigheid worden gemaakt, vanwege bijvoorbeeld verschillen in studie- en patiëntkenmerken en referentiewaarden.

Sterke en zwakke punten van de SCORE-studie

Een prospectieve cohortstudie met opeenvolgende patiënten met een beroerte die revalideren, is ideaal om in deze specifieke patiëntengroep de resultaten op lange termijn te bestuderen. De omvang van de steekproef is een sterk punt van de SCORE-studie, omdat deze studie een relatief groot aantal patiënten met een beroerte bevat (901 in 2021) in vergelijking met andere cohortstudies. Omdat deze studie alleen patiënten die gebruik maakten van multidisciplinaire klinische of poliklinische revalidatie includeerde, geeft deze studie bovendien een diepgaand inzicht in de uitkomsten en het verloop van revalidatie bij deze specifieke subgroep van patiënten met een beroerte. De follow-up duur van 30 maanden na de start van de revalidatie geeft inzicht in het verloop van verschillende uitkomstmaten op de lange termijn. Vanuit klinisch oogpunt is een lange follow-up duur van belang, omdat de duur van routinematige follow-up meestal beperkt is. Daardoor zijn zorgverleners in de revalidatie over het algemeen niet op de hoogte van de uiteindelijke uitkomsten van hun behandeling. Ook kunnen op de langere termijn mogelijk nieuwe problemen optreden of aanwezige problemen verergeren, wat mogelijk een nieuwe indicatie vormt voor consultatie van een revalidatiearts. Een ander sterk punt is het brede scala van uitkomsten, inclusief relatief weinig bestudeerde aspecten, zoals pijn, patiënt activatie en kosten.

De opzet van een groot prospectief cohortonderzoek maakt het ook mogelijk om daarin studies onder te brengen (z.g. nested studies) die er op gericht zijn om de effectiviteit van interventies te evalueren. Studies met een pre-test post-test design zijn daarvan een voorbeeld. Daarbij worden de uitkomsten vergeleken tussen patiënten die zijn opgenomen in een periode waarin een interventie niet werd toegepast en in een periode waarin deze wel werd toegepast. Deze methodologie werd bijvoorbeeld gebruikt in de Fit After Stroke (FAST)@Home-studie[14]. Dat

onderzoek evalueerde de effectiviteit van een e-health platform door efficiënt gebruik te maken van de gegevens die waren verzameld in het kader van de lopende SCORE-studie[14].

Meer kennis over de subgroep van patiënten met een beroerte die gebruik maken van multidisciplinaire revalidatie is waardevol, maar kan ook beschouwd worden als een beperking. Uitbreiding van de cohortstudie naar alle patiënten met een beroerte zou inzichten kunnen opleveren over verschillen en overeenkomsten in uitkomsten van patiënten die na ziekenhuisopname naar huis gaan of opgenomen worden voor geriatrische revalidatie. Met dat doel is de SCORE+ studie ontwikkeld. Deze studie includeerde van september 2020 tot september 2021 342 patiënten in het Haaglanden Medisch Centrum (onder leiding van HJ Arwert, K Jellema, SJ Tamminga en TPM Vliet Vlieland).

Een andere beperking met betrekking tot de selectie van patiënten is dat patiënten met ernstige afasie en anderszins ernstig aangedane patiënten niet deelnamen, omdat zij niet in staat waren om vragenlijsten in te vullen. Daarnaast moesten de behandelende artsen de patiënten persoonlijk uitnodigen voor het onderzoek. Dit creëerde een drempel, waardoor het mogelijk was dat sommige patiënten die in aanmerking kwamen, werden gemist. Een andere vorm van selectie deed zich voor bij de analyses. In sommige studies in dit proefschrift werden de analyses uitgevoerd binnen een subgroep van patiënten, namelijk degenen die de follow-up afmaakten en/of een specifieke vragenlijst invulden. In een aantal analyses werd gevonden dat de patiënten die de gehele studie doorliepen verschilden van degenen die dat niet deden met betrekking tot vaker alleen wonen, een eerder doorgemaakt hartinfarct, alcoholgebruik, een hogere mate van kwetsbaarheid en opleidingsniveau[8,15].

Een andere beperking van de studie betreft de interventie, multidisciplinaire revalidatie, zelf. Ondanks de beschikbaarheid van richtlijnen[16,17] is de multidisciplinaire klinische of poliklinische revalidatie weinig gestandaardiseerd en de daadwerkelijk geleverde zorg wordt niet altijd of niet volledig vastgelegd op het niveau van de individuele patiënt. Een eerdere vergelijking van de structuur (vier centra)[7] en processen (twee centra)[18] van de revalidatiezorg na een beroerte vond significante verschillen tussen centra. Met betrekking tot de structuur van de revalidatie was er een verschil in opname- en ontslagcriteria, de aanwezigheid en samenstelling van subgroepen van patiënten, de aanwezigheid en duur van zorgpaden, de timing van de teamvergaderingen, het tijdstip van klinische metingen, de maximale tijd tussen ontslag uit het ziekenhuis en opname, de inhoud van de modules die gaan over nazorg en over terugkeer naar werk, welke medische en paramedische disciplines beschikbaar zijn, faciliteiten voor behandeling en diagnostiek en strategieën voor betrokkenheid van de mantelzorger[7]. Met betrekking tot het zorgproces werden verschillen gezien in het aantal uren logopedie, psychologie en activiteitenbegeleiding. Het bleek echter dat de uitkomsten van revalidatie over het algemeen vergelijkbaar waren[18].

Ten slotte, de belasting voor de patiënten om alle vragenlijsten en vragen op meerdere meetmomenten in te vullen is de keerzijde van het verzamelen van een schat aan gegevens. Idealiter worden de gegevens niet naast de zorg verzameld maar in het kader van zorg, en kunnen door zorgverleners en patiënten worden gebruikt om behandeldoelen vast te stellen en te evalueren.

Onderzoekspartners

Naast de bovengenoemde sterke punten van de SCORE-studie is er nog een ander aspect dat het waard is om afzonderlijk vermeld te worden: de betrokkenheid van onderzoekspartners. Om er voor te zorgen dat de opzet van de SCORE-studie, inclusief de onderzoeksvragen, relevant was voor patiënten met een beroerte en hun naasten werd vanaf het begin van de studie een panel van onderzoekspartners betrokken[19]. Patiëntparticipatie in onderzoek is belangrijk, omdat de perspectieven van iedereen die belang heeft bij de uitkomsten van het onderzoek moeten worden meegenomen, waarmee de relevantie en impact van het onderzoek worden vergroot[20,21].

Het panel van onderzoekspartners van de SCORE-studie bestond uit acht patiënten en één naaste. Deze patiënten hadden een beroerte of niet aangeboren hersenletsel, hadden klinisch en/of poliklinisch bij Basalt gerevalideerd en waren gemotiveerd om hun perspectief te delen en zo het onderzoek te verbeteren. In de periode 2013 tot nu kwamen de onderzoekspartners en de onderzoekers één of twee keer per jaar bijeen. Als belangrijke punten werden onder andere veranderingen en behoeften op de lange termijn na een beroerte en de terugkeer naar werk genoemd. Dit resulteerde in toevoeging van nieuwe onderzoeksvragen en methoden aan het protocol. De onderzoekspartners hebben ook geholpen bij de voorbereiding van de SCORE-dag die 2019 die in Leiden en Den Haag werd gehouden. De SCORE-dag werd georganiseerd ter ere van het vijfjarig bestaan van de SCORE-studie. Op deze dag werden alle deelnemers aan het onderzoek geïnformeerd over de resultaten van de SCORE-studie. De SCORE-dag werd in Leiden bezocht door 90 patiënten en hun naasten en in Den Haag door 123 patiënten en naasten. Zij hadden veel waardering voor het delen van de resultaten van het onderzoek en het uitwisselen van ervaringen met medepatiënten en naasten.

Vanwege de waardevolle bijdrage van de onderzoekspartners aan de SCORE-studie is dit concept binnen Basalt verder uitgebreid naar andere studies en is een nieuw panel gevormd: de innovatiepartners. De innovatiepartners geven hun input over eHealth innovaties en de implementatie daarvan in de revalidatiezorg. Ze zijn betrokken bij het opstellen van plannen over eHealth, bij het helpen ontwikkelen en testen van innovaties en bij het geven van kritische adviezen. Deze betrokkenheid zal zorgen voor een succesvollere implementatie van eHealth in de revalidatiezorg.

Meetinstrumenten

Om de uitkomst van belang goed te kunnen meten, moet een meetinstrument adequate meeteigenschappen hebben[22]. Voor een aantal instrumenten die worden aanbevolen in de ICHOM Standard Set for Stroke en de MDS-ABI zijn niet alle meeteigenschappen, interpreteerbaarheid en afkapwaarden bij patiënten met een beroerte bekend. Zo zijn de inhoudsvaliditeit, criteriumvaliditeit en cross-culturele validiteit/meetinvariantie van de PROMIS Global Health niet onderzocht bij patiënten met een beroerte[23].

Voor de evaluatie van een behandeling is de responsiviteit, dat wil zeggen het vermogen van een meetinstrument om verbetering of verslechtering vast te leggen, een belangrijke meeteigenschap[22]. In dit proefschrift werd de responsiviteit van de USER geëvalueerd door de effectgrootte (ES) en het gestandaardiseerde responsgemiddelde (SRM) te berekenen bij patiënten met een beroerte tussen opname en ontslag in het revalidatiecentrum en deze te vergelijken met die van de Barthel index. Hoewel met de ES en SRM enig inzicht in de responsiviteit kan worden verkregen, moet worden opgemerkt dat de meest adequate methode om de responsiviteit van een meetinstrument te evalueren een beoordeling van de longitudinale validiteit moet bevatten. Net als bij constructvaliditeit moet de longitudinale validiteit worden beoordeeld door vooraf bepaalde hypothesen te toetsen. Bijvoorbeeld over verwachte correlaties tussen veranderingen in metingen of verwachte verschillen in veranderingen tussen "bekende" groepen[22]. Een zwak punt van deze methode betreft het formuleren van hypothesen. Daarbij kunnen de verwachtingen over de sterkte van de correlaties tussen onderzoekers verschillen. Aangezien in onze studie geen gebruik werd gemaakt van een beoordeling van de longitudinale validiteit moeten de conclusies met enige voorzichtigheid worden geïnterpreteerd.

Een uitdaging met betrekking tot de optimale samenstelling van de set uitkomstmaten is de mogelijke spanning tussen de belangrijkste doelstellingen van de metingen: voor individuele patiëntenzorg of voor kwaliteit van zorg, binnen of tussen instellingen. Voor een aantal generieke meetinstrumenten zijn de relevante meeteigenschappen bij specifieke patiëntengroepen onvoldoende vastgesteld. Een voorbeeld daarvan is dat het onzeker is of de PAM geschikt is voor patiënten met een beroerte die gebruik maakten van revalidatie (**hoofdstuk 5**). In het algemeen ontbreken voor veel instrumenten de afkapwaarden om individuele patiënten met verschillende niveaus van gezondheidsproblemen en zorgbehoeften te onderscheiden, waardoor de bruikbaarheid in individuele patiëntenzorg beperkt is. Een specifiek nadeel van generieke meetinstrumenten is dat zij mogelijk niet relevant, volledig en te begrijpen zijn voor patiënten met een specifieke aandoening, zoals een beroerte.

Implicaties voor onderzoek

De SCORE-studie heeft in het algemeen aangetoond dat het meten van veel uitkomstmaten ook op lange termijn bij patiënten met een beroerte die klinisch of poliklinisch revalideerden, haalbaar is en waardevolle inzichten verschaft[8].

Gezien de eerder genoemde sterke en zwakke punten van de SCORE-studie kunnen een aantal aanbevelingen voor de voortzetting van deze studie worden gedaan die ook van toepassing zouden kunnen zijn op andere observationele cohortstudies:

1) Het wervingsproces kan worden vergemakkelijkt door de administratieve activiteiten voor de behandelend artsen die nodig zijn om de patiënten uit te nodigen te verminderen; op deze manier kan het missen van patiënten om logistieke redenen worden verminderd; 2) De set vragenlijsten moet worden beperkt en vereenvoudigd, zodat de bereidheid tot deelnemen en de respons percentages met betrekking tot het invullen zullen toenemen; 3) De optimale samenstelling van de set meetinstrumenten kan worden heroverwogen, mede gebaseerd op de instrumenten die worden geadviseerd in de ICHOM Standard Set for Stroke en/of de MDS-ABI. Op dit moment worden aanbevelingen voor uitkomstmaten in de beroertezorg in Nederland ontwikkeld in het kader van het nationale programma Uitkomstgerichte Zorg[24]. Ook hiermee moet rekeningen worden gehouden. Daarnaast zijn er vanuit een internationaal perspectief initiatieven om de kwaliteit van de revalidatiezorg te monitoren door de responsiviteit te beoordelen van een nieuw ontwikkelde set om kwaliteit te meten voor revalidatie[25]; 4) Om het aantal in te vullen vragen te beperken kan het gebruik van CAT (Computer Adaptief Testen)-versies van vragenlijsten worden overwogen. Voor een aantal PROMIS-instrumenten zijn zulke formats beschikbaar; 5) Aangezien communicatieproblemen veel voorkomen bij patiënten met een beroerte zou de toevoeging van een aantal klinische testen kunnen worden overwogen. Dat vereist wel voldoende middelen voor de tijd en andere kosten voor het afnemen van dergelijke testen. Een andere mogelijkheid is het gebruik van vragenlijsten die door alle patiënten kunnen worden ingevuld ondanks communicatieproblemen. Dergelijke vragenlijsten waarbij gebruikt wordt gemaakt van digitale technologie worden momenteel ontwikkeld[26].

Naast de keuze van de geschikte meetinstrumenten zijn er nog andere uitdagingen met betrekking tot onderzoek in een populatie van patiënten met een beroerte die gebruik maakten van revalidatie. Voor revalidatie in het algemeen is de evidentie voor de (kosten)effectiviteit van specifieke interventies die deel uitmaken van een multidisciplinair behandelprogramma schaars. In de revalidatiezorg na een beroerte lijkt er sprake te zijn van praktijkvariatie[7,18]. Deze bevinding wijst mogelijk op suboptimale zorgverlening. Om de “black box” te ontrafelen is meer onderzoek naar de (kosten)effectiviteit van specifieke multidisciplinaire revalidatie interventies of behandelstrategieën nodig. Bijvoorbeeld door de uitkomsten (effectiviteit,

kosten en tevredenheid van patiënten en zorgverleners) van verschillende zorgpaden voor patiënten met specifieke patronen van problemen en beperkingen te vergelijken.

De beschikbaarheid van een lopend cohortonderzoek op meerdere locaties kan de uitvoering van dergelijk onderzoek vergemakkelijken. Dit maakt de efficiënte uitvoering van zowel pre-test post-test studie als randomized clinical trials mogelijk. Voor de uitvoering van dit soort studies is het echter van belang dat de aard en frequentie van aangeboden interventies nauwkeurig op patiënt niveau worden geregistreerd. Deze registratie behoeft verbetering.

Implicaties voor de klinische praktijk

Metingen tijdens revalidatie

De resultaten van de studies die in dit proefschrift worden gepresenteerd, suggereren dat bij patiënten met een beroerte die gebruik maakten van multidisciplinaire revalidatie meer aandacht nodig is voor de diagnose en behandeling van pijn in de bovenste extremiteit, het bevorderen van terugkeer naar werk en van andere manieren van betekenisvolle participatie als terugkeer naar betaald werk onhaalbaar lijkt en het verhogen van de patiënt activatie als voorwaarde voor effectief zelfmanagement[27]. Daarnaast werd ook vastgesteld dat een aanzienlijk deel van de naasten een hoge mantelzorgerlast ervaart[28].

Deze verhoogde aandacht mag niet beperkt blijven tot het onderkennen van deze problemen, maar moet ook leiden tot het invoeren van adequate interventies. Het is denkbaar dat de subacute fase niet het optimale moment is voor sommige van deze interventies. In dat geval is een adequate overdracht aan zorgverleners in de poliklinische revalidatie of eerstelijnsgezondheidszorg van groot belang. Door de bovengenoemde onderwerpen op te nemen in bijvoorbeeld zorgpaden of richtlijnen, zal het bewustzijn van het belang van deze elementen toenemen. De toevoeging van door de patiënt gerapporteerde uitkomstmaten in routinematige werkstromen zou kunnen helpen bij het identificeren van onderwerpen waar ondersteuning nodig is.

Follow-up na revalidatie

In Nederland is op dit moment de follow-up na ontslag van multidisciplinaire revalidatie meestal tijdelijk (6-12 maanden), terwijl de resultaten van dit proefschrift suggereren dat op lange termijn beperkingen aanwezig kunnen blijven, verergeren en ook nieuwe beperkingen kunnen ontstaan. Sommige beperkingen, zoals die in participatie worden pas op langere termijn duidelijk, zoals blijvende arbeidsongeschiktheid die bij veel patiënten pas na twee jaar ziekteverlof definitief is. Verder bleek uit dit proefschrift dat pijn en belasting van de mantelzorger op de lange termijn kunnen ontstaan[28]. Verbeteringen van de huidige zorg zouden kunnen bestaan uit structurele lange termijn metingen om patiënten met een risico

op verslechtering te identificeren. Het opzetten van een surveillancesysteem zou in nauwe samenwerking met bijvoorbeeld huisartsen, gespecialiseerde CVA-verpleegkundigen die in een wijkteam werken of fysiotherapeuten moeten plaatsvinden[29], omdat is gebleken dat het langdurige gebruik van zorg in de eerste lijn aanzienlijk was. Daarnaast moeten huisartsen en CVA-verpleegkundigen weten naar welke paramedici en revalidatieartsen zij patiënten met een beroerte kunnen doorverwijzen. In de regio Zuid-Holland zijn ergotherapeuten, fysiotherapeuten en logopedisten met ervaring met patiënten met neurologische aandoeningen in de eerstelijnszorg verenigd in een netwerk (Neuronet) om de zorg voor patiënten met neurologische aandoeningen te borgen en mogelijk te verbeteren[30].

In het algemeen vulde dit proefschrift enkele kennislacunes over lange termijn uitkomsten na revalidatie na een beroerte. Het onderzoek heeft ondanks nieuwe inzichten laten zien dat er op dit gebied nog veel uitdagingen zijn, zowel wat betreft onderzoek als in de klinische praktijk.

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Chapter 10

List of publications

Curriculum Vitae

Dankwoord

List of publications

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van Meijeren-Pont W, Tamminga SJ, Fiocco M, Gonzalez Avila, Volker G, Janssen SMJ, Vliet Vlieland TPM, Oosterveer DM; SCORE Study Group. Patient activation during the first 6 months after the start of stroke rehabilitation.
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Accepted for publication in Disabil Rehabil.

van Meijeren-Pont W, van Velzen JM, Volker G, Arwert HJ, Meesters JJL, de Kloet AJ, van Bennekom CAM, Vliet Vlieland TPM, Tamminga SJ, Oosterveer DM, on behalf of the Stroke Cohort Outcomes of REhabilitation (SCORE) study group. The long-term course of participation in stroke patients with paid employment.
Submitted.

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Groeneveld IF, Goossens PH, **van Meijeren-Pont W**, Arwert HJ, Meesters JJL, Rambaran Mishre AD, Van Vree F, Vliet Vlieland TPM; SCORE-study group. Value-based stroke rehabilitation: feasibility and results of patient-reported outcome measures in the first year after stroke.
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Curriculum Vitae

Wilhelmina (Winke) van Meijeren-Pont werd geboren op 2 augustus 1989 in Alphen aan den Rijn. In 2007 behaalde zij haar VWO eindexamen aan het Groene Hart Lyceum in Alphen aan den Rijn en werd zij ingeloot voor de studie Fysiotherapie aan de Hogeschool Leiden. Winke heeft haar afstudeeronderzoek naar de inhoud van revalidatiedoelen en -meetinstrumenten bij patiënten met reumatoïde artritis, gebruikmakend van de International Classification of Functioning, Disability and Health, uitgevoerd in het Leids Universitair Medisch Centrum (LUMC) onder leiding van dr. Jorit Meesters. In 2011 behaalde zij de Bachelor Fysiotherapie. Aansluitend heeft Winke een pre-master Bewegingswetenschappen gedaan aan de Vrije Universiteit te Amsterdam. In 2012 is zij gestart met de Master Bewegingswetenschappen die zij in 2014 heeft afgerond. Daarnaast heeft Winke van 2012 tot 2020 als fysiotherapeut gewerkt in verschillende fysiotherapie praktijken in Alphen aan den Rijn en Leiden.

In oktober 2016 is Winke, naast haar werkzaamheden als fysiotherapeut, gestart als junior onderzoeker bij het Stroke Cohort Outcomes of REhabilitation (SCORE)-onderzoek bij het toenmalige Rijnlands Revalidatie Centrum (RRC) in Leiden en Sophia Revalidatie in Den Haag, inmiddels gefuseerd tot één organisatie, Basalt. In November 2018 ving zij aan met het promotietraject ‘Comprehensive measurement of long term outcomes and costs of rehabilitation in patients with stroke’ bij het LUMC, in samenwerking met Basalt, onder leiding van prof. dr. Thea Vliet Vlieland, dr. Diana Oosterveer en dr. Sietske Tamminga.

Momenteel is Winke betrokken bij het vervolg van het SCORE-onderzoek. Naast deze onderzoekstaken is Winke betrokken bij het organiseren van het wetenschappelijk onderwijs voor de artsen in opleiding tot specialist revalidatiegeneeskunde binnen Basalt. Daarnaast is zij betrokken bij de dataverzameling van het project ikoefenzelf.nl, gericht op de ontwikkeling en implementatie van een platform voor digitale interventies om ondersteuning op maat te bieden aan CVA patiënten bij hun revalidatie thuis.

Winke is getrouwd met Martin van Meijeren. Samen hebben ze een zoon, Thijs (2020).

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