

How to cope with stroke?

The effectiveness of Problem Solving Therapy

Marieke Visser

The research described in this thesis was funded by the National Initiative Brain and Cognition (NIBC; this quick result project is embedded in the pillar “The Healthy Brain, Program Cognitive Rehabilitation” [grant number 056-11-010]), Stichting Coolsingel, and Erasmus MC Cost-Effectiveness Research.

Financial support by the Dutch Heart Foundation and Rijndam Revalidatie for the publication of this thesis is gratefully acknowledged.

ISBN: 978-94-6299-344-0

Printed by: Ridderprint BV - www.ridderprint.nl

Layout: Ridderprint BV - www.ridderprint.nl

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How to Cope with Stroke? The effectiveness of Problem Solving Therapy

Hoe om te gaan met CVA? De effectiviteit van Problem Solving Therapy

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de rector magnificus

Prof.dr. H.A.P. Pols

en volgens het besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
dinsdag 21 juni 2016 om 13.30 uur

door

Marieke Margaretha Visser
geboren te Alkmaar

PROMOTIECOMMISSIE

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General Introduction

CHAPTER 1

Stroke is a global and increasing public health problem. In the Netherlands approximately 44,000 people suffer a stroke every year.¹ With the development and improvement of medical and surgical technologies, the mortality rate after stroke has decreased over the years, whereas stroke morbidity has increased. After stroke, approximately 75% of surviving patients will have problems in mobility, fatigue, emotion, and cognition, measured up to five years post stroke. In many patients with stroke these long-term consequences in daily life result in decreased health-related quality of life (HR-QoL).² Even after seven years, a large proportion of patients with stroke report a poor HR-QoL.³ The World Health Organization Quality of Life (WHOQOL) Group defines quality of life as “individuals’ perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”,⁴ HR-QoL refers to the health-related aspects of quality of life. To quantify HR-QoL, so called ‘utility scores’ can be used. These scores range along a continuum from 0 (equal to death) to 1 (equal to full health). Utility scores for HR-QoL after stroke are in the range of 0.47 to 0.68, which is substantially lower than those of a healthy reference population (score 0.93).^{5,6} HR-QoL after stroke is predicted by several factors, including functional constraints, age, sex, socioeconomic status, depression and coping strategy.⁷⁻¹⁰

HR-QoL changes over time after stroke. During post-acute stroke rehabilitation HR-QoL will increase, along with recovery of bodily functions and activities.¹¹ Discharge from rehabilitation seems a challenging time with respect to HR-QoL. When treatment is completed, patients are confronted with the consequences of stroke in their home environment. Patients need to cope with these consequences without professional support, which can cause psychological distress. Therefore, after discharge from rehabilitation HR-QoL may decrease,¹¹ with even a further decline in the long-term.¹²

COPING, PROBLEM SOLVING, DEPRESSION AND HR-QOL AFTER STROKE

An important psychosocial variable related to HR-QoL is depression, which is commonly present after stroke; the estimated first year prevalence is 33%.¹³ The cumulative incidence of depression is shown to be up to 52% within five years after stroke.¹⁴ Depression has a negative effect on HR-QoL after stroke,¹⁴⁻¹⁶ and appears to be more influential than functional constraints.¹⁵

Another psychosocial factor related to HR-QoL is coping strategy. Coping is defined as the cognitive and behavioral efforts to deal with stressful situations and the emotions they generate.^{17,18} In literature there are several coping theories;

e.g. problem-solving vs emotion-focused strategies, avoidance-oriented vs active approach-oriented coping, assimilative vs accommodative coping.^{19,20} Regarding coping after stroke, it is known from literature that patients with stroke insufficiently use active, problem-oriented coping strategies, while active coping strategies are associated with better HR-QoL.^{21,22} Furthermore, coping becomes more important in determining HR-QoL after stroke over time, while the importance of general functioning decreases.¹⁰ This implies that in the long-term, patients could benefit from improved coping. Coping can be influenced by means of intervention.²³ No studies have investigated the effect of an intervention on HR-QoL through the change of coping strategies in patients with stroke.

A specific coping process is problem solving, which is defined as “the process of finding solutions to specific problems”.¹⁸ Problem solving cannot be directly compared with or distinguished from other coping activities because it can serve a variety of coping functions. Problem solving has been shown to be related with depression and HR-QoL,^{24,25} and has been shown helpful during the phase of recovery after discharge from stroke rehabilitation, when HR-QoL decreases.²²

PROBLEM SOLVING THERAPY

Problem Solving Therapy (PST) is a low cost intervention aimed at coping strategies; patients are taught to increase structure in solving problems and flexibility by using different coping strategies in various situations. PST is a widely used intervention and has been investigated in several patient populations; e.g. patients with depression,^{26,27} breast cancer survivors,^{28,29} and patients with chronic obstructive pulmonary disease.³⁰ In patients with stroke, PST has been shown successful in reducing symptoms of depression³¹ and in preventing post-stroke depression,³² although the latter effect was not significant using more conservative analysis. The effects of PST on coping strategy and HR-QoL after stroke are unknown.

The aim of this thesis is to evaluate whether PST, administered as an add-on module in outpatient stroke rehabilitation, is effective in improving coping strategy and HR-QoL after finishing the rehabilitation program. The PST intervention has been slightly adapted for our study; it is provided in an open group design requiring a continuous flow of patients entering and leaving the group. The intervention consists of eight group sessions of 1.5 hours a week, with homework exercises after each session. The group consists of three to six participants and is provided by a trained neuropsychologist. The problem solving process is structured in four steps: [1] define problem and goal; [2] generate multiple solutions; [3] select a solution; and [4] implement and evaluate.

AIM OF THIS THESIS

The aim of this thesis is to evaluate the effectiveness of PST for patients in the rehabilitation phase after stroke. In order to do so, we aim to [1] investigate the relationships between coping strategy, problem solving skills, depression and HR-QoL after stroke and [2] to evaluate the effect of PST on coping strategy and HR-QoL. Finally, we want to [3] evaluate the effectiveness of other stroke rehabilitation interventions on HR-QoL.

As described, depression and coping both are important psychosocial determinants for HR-QoL, but these variables have been shown to be related to each other as well. Depression is a known effect modifier of the relation between coping strategy and HR-QoL.³³ Therefore, this thesis investigates the relationship between coping, depression and HR-QoL after stroke in different phases of recovery. In **Chapter 2**, the relative association of coping strategy and depression with HR-QoL in patients in the chronic phase after stroke is investigated. This study included a sample of 213 patients >18 months after stroke. In **Chapter 3**, we assess whether coping strategy and problem solving skills are related to psychosocial HR-QoL, independent of depression. In addition, we describe whether patients with high and low depression scores after stroke use different coping strategies and problem solving skills. This study included a sample of 166 patients in the rehabilitation phase after stroke.

Chapter 4 presents the study protocol of a pragmatic randomized controlled trial (RCT) we set up to evaluate the effectiveness of PST during outpatient stroke rehabilitation. Both the content of the intervention and the design and methods of the study are described. The results of this RCT, up to 12 months after the intervention, are presented in **Chapter 5**.

Since we were interested in the beneficial effect of PST on HR-QoL, which is the ultimate outcome measure in rehabilitation, we questioned whether other therapies could also improve HR-QoL after stroke. In **Chapter 6**, the results of a meta-analysis on the effectiveness of different types of stroke rehabilitation interventions on HR-QoL are described. This meta-analysis aimed to synthesize evidence from the literature about the effectiveness of rehabilitation interventions after stroke, and to evaluate which type of intervention is most effective.

Finally, **Chapter 7** presents a general discussion of the results and conclusions of this thesis. Methodological issues are discussed, as well as implications for clinical practice and future perspectives.

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CHAPTER 2

The relative effect of coping strategy and depression on health-related quality of life in patients in the chronic phase after stroke

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Objective

To investigate the relative associations of coping strategy and depression on health-related quality of life in patients in the chronic phase after stroke.

Design

Cross-sectional study.

Subjects

A total of 213 patients after stroke (>18 months post-onset), mean age of 59 years (standard deviation (SD) 9.86 years), 56% men, mean time post-stroke 53 months (SD 37.8 months).

Methods

Coping strategy was measured using the assimilative-accommodative coping scale, depression using the Center for Epidemiologic Studies Depression Scale, and quality of life using the World Health Organization Quality of Life-BREF. Multivariable regression analyses were performed, adjusted for patient characteristics.

Results

Depression score was independently related to all domains of quality of life (Psychological Health ($\beta=-0.924$; $p=0.000$), Physical Health ($\beta=-0.832$; $p=0.000$), Social Relationships ($\beta=-0.917$; $p=0.000$), Environment ($\beta=-0.662$, $p=0.000$)). Accommodative coping ($\beta=0.305$; $p=0.024$) and assimilative coping ($\beta=0.235$; $p=0.070$) were independently related to the domain Psychological Health, adjusted for depression and education level.

Conclusion

Coping strategies and depression score were independently associated with Psychological Health in patients in the chronic phase after stroke. Patients who prefer an accommodative coping strategy may show less symptoms of depression. Preferable coping strategies may be trained in order to improve both depression score and health-related quality of life in future research.

INTRODUCTION

The World Health Organization Quality of Life (WHOQOL) Group defines quality of life as “individuals’ perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”.¹ Health-related quality of life (HR-QoL) refers to the health-related aspects of quality of life. On average, utility scores of HR-QoL after stroke range from 0.47 to 0.68 (utility score equal to death is 0.0 and full health 1.0), which is lower than the value of a healthy reference population (utility score 0.93).^{2,3} Even after 7 years, a large proportion of patients report a poor HR-QoL.⁴ HR-QoL after stroke is predicted by functional constraints, age, gender, and psychosocial factors, such as depression and socioeconomic status.^{2,5-7} Depression is common after stroke, with an estimated first year prevalence of 30%, and it appears to be more influential than functional constraints.⁸ A recent systematic review showed a cumulative incidence of depression of up to 52% within 5 years after stroke. Lower quality of life was an outcome of depression in this study.⁹

Another important psychosocial factor with regard to HR-QoL after stroke is coping style.¹⁰⁻¹³ Coping style is commonly defined as someone’s preferred way of dealing with stressful situations. There are several dominant coping theories in literature; problem-solving vs emotion-focused strategies, avoidance-oriented vs active approach-oriented coping, and dispositional vs situational approaches to coping.¹⁴ Brandstädter & Renner (1990) use different dimensions; they distinguish two general coping strategies: assimilative and accommodative coping.¹⁵ Patients applying the assimilative coping strategy aim to adjust the situation to their personal preferences, trying to continue life as it was before an unpleasant event. This strategy is also called tenacious goal pursuit. Patients applying the accommodative coping strategy aim to adjust their personal preferences to the situation, accepting the consequences of an event. This strategy is also called flexible goal adjustment.¹⁵ According to Brandstädter & Renner (1990) both coping strategies may operate simultaneously. However, they expect that assimilative coping is dominant in the acute phase after an unpleasant event, whereas accommodative coping gradually increases over time. In patients after stroke, these coping strategies have been shown to be related to quality of life. Smout et al. (2001) shows that accommodative coping is related to a higher quality of life in patients in the chronic phase after stroke, while assimilative coping is related to a lower quality of life.¹³ Darlington et al. (2007) shows that, depending on the time post-onset, both assimilation and accommodation are positively related to quality of life from a societal perspective, with patients applying both strategies in different situations being most successful.¹¹

Coping strategy and depression have also been shown to be related. The assimilative and accommodative coping strategies are inversely related to symptoms of depression in a population of healthy adults.¹⁵ In patients after stroke, the use of avoidance coping was a predictor of depression before discharge from rehabilitation.¹⁶ This is an important finding, because stroke patients make less use of active problem-oriented coping than other brain-damaged patients and thus may be at higher risk of developing depression.¹⁷

Depression and coping are important variables that interact and that both may affect HR-QoL after stroke. A few studies investigated the influence of these two psychosocial factors on HR-QoL after stroke. One study showed that depression is related to a decreased HR-QoL in patients who have had an aneurysmal subarachnoid haemorrhage (SAH).¹⁸ These results may not apply to patients with ischemic and haemorrhagic strokes, as patients with SAH differ in age and comorbidity. Furthermore, this study in SAH patients only measured passive coping, which was not significantly associated with HR-QoL.¹⁸ A literature review described that depression and coping strategies are both determinants of HR-QoL after stroke.¹⁹ This review did not report the relative contribution of the two psychosocial factors. If coping independently affects HR-QoL after stroke, an intervention aimed at optimizing coping strategies may be useful in stroke rehabilitation programs. Therefore, the aim of the present study was to assess the relative effect of coping strategy and depression on HR-QoL in patients in the chronic phase after stroke. Because we focused on patients in the chronic stage after stroke, we expected that the accommodative coping strategy (flexibility: accepting the consequences of an event) would be more prevalent than the assimilative coping strategy (tenacity: adjusting the situation) in line with Brandtstädter & Renner (1990).¹⁵ Based on the literature we expected that depression is associated with a lower HR-QoL after stroke, and that an accommodative coping strategy is related to a higher HR-QoL. Despite the inverse relationship between coping strategy and depression, we hypothesized that the relationship between coping strategy and HR-QoL is independent of depression.

METHODS

Study design

Patients in the chronic phase after stroke (at least 18 months post-onset) were invited to participate in the study, from April 2008 to September 2010. The participants were former patients of Rijndam Rehabilitation Center in Rotterdam and Heliomare

Rehabilitation Center in Wijk aan Zee, both cities in the Netherlands. Inclusion criteria were: “first and only stroke”, a minimum of 18 months post stroke, age between 18 and 80 years, and living independently. Exclusion criteria were: progressive neurological disorders, such as dementia or multiple sclerosis, insufficient understanding of the Dutch language, alcohol or drug abuse, subarachnoid haemorrhage, or subdural haematomas. Eligible patients were approached by their physician and invited to participate in an intervention study to evaluate the effect of a memory training program.¹⁹ Patients were asked whether they subjectively experienced problems in memory functioning as a result of stroke. All patients were included for the baseline measurement, with or without subjective memory problems. The baseline data of this trial were used for this cross-sectional study. Approval was given by the medical ethics committee of the Erasmus MC. Written informed consent was obtained from all participants prior to the study.

Measurement instruments

Patients were assessed at home by a trained research psychologist. Coping strategy was measured using the assimilative-accommodative coping scale (AACCS).¹⁵ The AACCS consists of two subscales: tenacious goal pursuit (assimilative coping; adjusting the situation to personal preferences) and flexible goal adjustment (accommodative coping; adjusting personal preferences to the situation). Each subscale contains 15 items measured on a 5-point rating scale, ranging from 0 to 4. A sum score was calculated for both subscales, ranging from 0 to 60. The assimilative and accommodative strategies may operate simultaneously, but people mostly show a preference for one of the two strategies, which may change over time. Higher scores on one of the subscales indicate more use of that coping strategy. The internal consistency and validity of the scales are good.¹⁵ The questionnaire was translated into Dutch.²⁰

HR-QoL was measured using the WHOQOL-BREF, which is a generic HR-QoL questionnaire.¹ We used the Dutch version of this questionnaire, which has been shown valid and reliable.²¹ The questionnaire consists of 26 questions resulting in four domains of HR-QoL: Physical Health (e.g. pain, sleep, energy, mobility, activities of daily living, dependence on medicinal substances or aids, work capacity), Psychological Health (e.g. feelings, cognition, self-esteem, beliefs), Social Relationships (e.g. personal relationships, social support, sexual activity) and Environment (e.g. freedom, home environment, financial resources, health and social care, transport). The items are measured on a 5-point rating scale, ranging from 1 to 5. The domain scores are calculated as the sum scores of items in the domains and are transformed to a 0-100 scale.

Depression was measured using the Center for Epidemiologic Studies Depression Scale (CES-D). This questionnaire consists of 20 items concerning depression, ranging from 0 to 3. Higher scores indicate more depressive symptoms, a score of 16 or higher is considered “depressed”.²² The questionnaire has a range from 0 to 60, and shows good internal consistency and validity in the Dutch population.²³

The presence and severity of aphasia was measured using the short version of the Token Test.²⁴ The validated scale ranges from 0 to 36, a score of 29 or lower indicates aphasic features.

Level of education was classified in a 7-level system, in which 1 refers to some years of basic primary education and 7 refers to a university degree or higher.²⁵ Demographic and clinical characteristics, such as the side and type of stroke, were obtained from patient records and a structured interview by the research psychologist prior to the measurement.

Statistical analyses

Descriptive statistics were used to determine patient characteristics and the responses on the questionnaires. A sample of non-responders available from one of the two participating rehabilitation centers was compared with the study sample for the variables age, gender, type of stroke, side of stroke and time post-onset. The preferred coping strategy of each patient was determined by calculating the ratio between the sum scores of the two coping strategies (accommodation divided by assimilation), a ratio higher than one indicates more use of accommodative coping. Correlation coefficients were calculated to investigate if the variables HR-QoL, coping strategy and depression score were interrelated, and were checked for multi-collinearity. We also studied the correlation of these variables with the following potentially confounding variables: age, gender, living without a partner, level of education (dichotomized into high school or more (≥ 5) vs lower than high school (< 5)), time post-onset, side of stroke, type of stroke, and aphasia.

Multivariable linear regression analyses were performed to investigate the relative contribution of the variables that were significantly correlated with at least one of the domains of HR-QoL ($p < 0.10$). We assumed that HR-QoL, as measured with the four domains of the WHOQOL-BREF (Psychological Health, Physical Health, Social Relationships, Environment), may depend on the depression score and coping strategy. Variables were entered into the model using a blockwise procedure. In the first block both coping strategies were forced into the model. In the second block depression score was entered into the model, to estimate if the contribution of coping on HR-QoL changed. In the third block the potentially confounding variables

were forced in the model, to adjust for possible confounders. The variance explained for each block (R^2 change) and its significance were estimated. P-values of 0.05 were considered statistically significant. Model assumptions of linearity, normality and homoscedasticity were checked. Analyses were performed in SPSS version 19.0.

RESULTS

Inclusion

A total of 1,121 patients were approached for participation in this study, of which 220 signed an informed consent form. Reasons for not participating in the study were non-response ($n=628$), negative response ($n=265$), and not meeting the inclusion criteria ($n=8$). Seven patients were excluded after the baseline measurement due to lack of comprehension of the questionnaires and inadequate yes/no responses; we could not analyze the data from these patients due to the high level of missing data as a result of cognitive impairments and aphasia. Therefore, data of 213 patients were analyzed. The WHOQOL-BREF and CES-D were completed by all patients, there was one patient missing on the AACCS. Of all patients, 73.7% reported subjective memory complaints. The sample of non-responders ($n=434$) was not significantly different compared with the study participants except for the variables age and time post stroke; non-participants were older (mean 60.9 years, SD 11.9, $p=0.041$) and the time post-stroke was longer (mean 76.5 months, SD 38.2, $p<0.001$) than study participants.

Table 1 shows patient characteristics and mean outcome scores of the study participants. The HR-QoL mean domain scores are lower than those of a Dutch norm population (Table 1).²⁶ In 73.1% of patients the accommodative coping strategy was more prominent than the assimilative coping strategy.

Table 1. Descriptive variables

Variable	N	%
Gender (male)	117	56
Educational level (high)	48	23.3
Partner (no)	50	23.9
Side of stroke (left)	110	53.7
Type of stroke (ischemic)	139	70.6
	Mean	SD
Age (years)	58.97	9.86
Time post stroke (months)	52.95	37.80
Aphasia severity ^a	30.60	6.56
Depression score ^b	11.83	10.16
Accommodative coping ^c	38.62	6.95
Assimilative coping ^c	33.25	6.16
Psychological Health ^d	63.27	16.25
Physical Health ^d	64.51	18.20
Social Relationships ^d	65.33	18.84
Environment ^d	69.66	14.55

^aMeasured using the Token Test

^bMeasured using the Center for Epidemiologic Studies Depression Scale

^cMeasured using the assimilative-accommodative coping scale

^dMeasured using the WHOQOL-BREF; norm scores: Psychological Health: 78.75; Physical Health: 89.38; Social Relationships: 73.75; Environment: 74.38.²⁶

Correlation coefficients

Pearson and Spearman correlation coefficients are shown in Table 2. There were no indications for multi-collinearity. The correlation coefficients showed that both depression and accommodative coping are strongly related to all four domains of HR-QoL (Table 2). Patients with a higher depression score had a lower HR-QoL and patients making more use of accommodative coping had a higher HR-QoL. The variables depression and the accommodative coping strategy were inversely related. Assimilative coping was only significantly related to the domains Psychological Health and Environment, patients making more use of assimilative coping had a higher HR-QoL in these domains. Living without a partner was negatively related

Table 2. Correlation coefficients

	Psychological Health	Physical Health	Social Relationships	Environment	Depression	Accommodative coping	Assimilative coping
Physical Health	r=0.600**						
Social Relationships	r=0.542**	r=0.412**					
Environment	r=0.674**	r=0.531**	r=0.561**				
Depression score	r=-0.689**	r=-0.513**	r=-0.527**	r=-0.554**			
Accommodative coping	r=0.456**	r=0.274**	r=0.300**	r=0.299**	r=-0.464**		
Assimilative coping	r=0.153*	r=0.056	r=0.089	r=0.138**	r=-0.045	r=0.067	
Age	r=0.112	r=0.064	r=-0.032	r=0.136*	r=-0.214**	r=0.211**	r=-0.029
Gender (male)†	r=-0.100	r=-0.157*	r=0.084	r=-0.083	r=0.073	r=-0.081	r=-0.014
Absence of partner‡	r=-0.167*	r=-0.151*	r=-0.234**	r=-0.327**	r=0.146*	r=0.040	r=-0.035
Educational level†	r=0.116	r=0.042	r=-0.073	r=0.168*	r=0.028	r=0.020	r=0.092
Time post-onset	r=-0.083	r=-0.066	r=-0.068	r=-0.092	r=0.036	r=0.020	r=-0.027
Side of stroke (left)†	r=-0.026	r=0.038	r=-0.047	r=-0.077	r=-0.034	r=0.015	r=-0.069
Type of stroke (ischemic)†	r=-0.081	r=-0.106	r=-0.058	r=-0.047	r=0.044	r=-0.084	r=-0.013
Aphasia severity	r=0.142*	r=0.026	r=0.113	r=0.242**	r=-0.056	r=0.086	r=0.092

**p-value ≤0.01 (2-tailed)

*p-value ≤0.05 (2-tailed)

†Spearman's rho correlation coefficients

to HR-QoL in all domains. Patients with a higher age or higher educational level had a higher HR-QoL in the domain Environment. Being a male was negatively related to the domain Physical Health. Patients who performed better on the test that measured aphasia had a higher HR-QoL in the domains Psychological health and Environment. Time post-onset, type of stroke and side of stroke were not related to any of the domains of HR-QoL, and were therefore not entered in the multivariable regression analysis.

Multivariable analysis

The significant variables were analysed further using multivariable regression analyses for the four domains of HR-QoL as dependent variables (Table 3). In the first block, accommodative coping was significantly related to all domains of HR-QoL. Assimilative coping was significantly related to Psychological Health. In the second block, both accommodative and assimilative coping were significantly related to Psychological Health, adjusted for depression score. Depression score was independently significantly related to all domains of HR-QoL. In the third block, depression score remained significantly related to all domains of HR-QoL (Psychological Health (B=-0.942; p=0.000), Physical Health (B=-0.832; p=0.000), Social Relationships (B=-0.917; p=0.000), Environment (B=-0.62, p=0.000)). Adjusted for depression and educational level, accommodative coping was significantly related to the domain Psychological Health (B=0.305; p=0.024). Assimilative coping (B=0.235; p=0.070) was borderline significant in the final model. In the other three domains of HR-QoL both accommodative coping and assimilative coping were no longer related with HR-QoL if depression was also included in the regression model. Living without a partner remained negatively related to the domains Social Relationships and Environment. Higher education also remained positively related to the domains Psychological Health and Environment. A better performance on the aphasia test was positively related to the domain Environment, independently of depression and the other independent variables.

Table 3. Multivariable linear regression analyses

	Psychological Health		Physical Health		Social Relationships		Environment	
	B	p-value	B	p-value	B	p-value	B	p-value
Block 1								
Accommodative coping	0.906	0.000	0.556	0.004	0.732	0.000	0.573	0.000
Assimilative coping	0.329	0.049	0.105	0.618	0.217	0.312	0.233	0.155
Block 2								
Accommodative coping	0.267	0.045	-0.014	0.943	0.093	0.627	0.076	0.599
Assimilative coping	0.290	0.027	0.070	0.709	0.178	0.343	0.203	0.154
Depression	-0.964	0.000	-0.860	0.000	-0.965	0.000	-0.750	0.000
Block 3								
Accommodative coping	0.305	0.024	0.036	0.854	0.246	0.191	0.134	0.327
Assimilative coping	0.235	0.070	0.051	0.789	0.105	0.562	0.103	0.434
Depression	-0.942	0.000	-0.832	0.000	-0.917	0.000	-0.662	0.000
Age	-0.116	0.175	-0.127	0.314	-0.233	0.054	0.027	0.754
Gender (male)	-1.426	0.393	-4.024	0.102	2.927	0.212	0.857	0.614
Absence of partner	-3.203	0.095	-3.630	0.197	-8.804	0.001	-8.738	0.000
Educational level (≥ 5 vs < 5)	4.129	0.029	0.565	0.837	-1.957	0.457	4.840	0.012
Aphasia severity	0.163	0.191	-0.045	0.806	0.231	0.188	-0.464	0.000
Model performance	%	p-value	%	p-value	%	p-value	%	p-value
R ² change block 1	0.176	0.000	0.044	0.013	0.075	0.001	0.084	0.000
R ² change block 2	0.324	0.000	0.189	0.000	0.221	0.000	0.227	0.000
R ² change block 3	0.030	0.045	0.021	0.359	0.073	0.001	0.121	0.000
R ² total	0.529		0.255		0.369		0.432	

DISCUSSION

This study confirmed our hypotheses that depression and accommodative coping (flexibility) are both independently related to Psychological Health in the chronic phase after stroke. Patients after stroke with a higher depression score had a lower HR-QoL, as expected based on earlier studies.^{27,28} Accommodative coping was an independent contributor to Psychological Health, adjusted for depression and level of education. This finding indicates that, independent of the presence of depressive symptoms, accommodative coping positively influences Psychological Health. Psychological Health incorporates facets such as feelings, cognition, self-esteem, and beliefs.¹ Patients with an assimilative coping strategy (tenacity) also had a higher HR-QoL in this domain. It appears that the ability to use both coping strategies, flexibility and tenacity, positively influences Psychological Health, which is in line with the findings of Darlington et al. (2007).¹¹

In all the other domains of HR-QoL, the accommodative coping strategy is also strongly related to HR-QoL, but not independent of depression. This may be caused by the inverse relationship between coping strategy and depression: patients who prefer an accommodative coping strategy show fewer symptoms of depression. Results of Schmitz et al. (1996) confirm this inverse relationship in a population of patients with chronic pain.²⁹ From this analysis we cannot conclude whether maladaptive coping strategies may lead to depression or vice versa. The domains Physical Health, Social Relationships and Environment appear to differ from the domain Psychological Health because these domains depend more on external factors. Other variables, such as severity of aphasia, living without a partner and higher education were more important than coping strategies in these domains.

This study suggests that coping strategy independently contributes to Psychological Health after stroke. Therefore, it might be beneficial to target patients' coping strategies in post-stroke rehabilitation programs. Backhaus et al. (2010) shows that an intervention was beneficial in changing maladaptive coping strategies in traumatic brain-injured patients.³⁰ In patients after stroke, Darlington et al. (2007) shows that with the passing of time, the importance of general functioning in determining HR-QoL diminishes, whereas coping becomes more important.¹¹ Coping strategies at discharge of rehabilitation were predictive of QoL after one year.¹² Depression is an important factor influencing HR-QoL after stroke, and should not be neglected. However, the current study suggests that coping strategy may be an important target in post-stroke rehabilitation, and might provide an entry to improve both HR-QoL and to decrease depressive symptoms.

The current study had some limitations that should be considered. A multivariable linear regression analysis was used to evaluate the predictive value of depression and coping strategy on HR-QoL, which assumes a causal relationship between the independent and dependent variables. Based on the literature, we assumed that HR-QoL depends on the psychosocial variables depression and coping strategy.¹⁰ However, as we used a cross-sectional study design, it is uncertain whether this assumption holds. To confirm our results, this relationship should be investigated further in a longitudinal study design in future studies. In addition, we used the assimilative-accommodative coping scale to measure coping strategy. Recently, results of a validation study on this questionnaire showed some evidence that the subscales may not clearly distinguish between the two strategies of coping in relatively healthy women.³¹ However, there is no consensus about which instrument should be used to measure coping after stroke.¹⁴ Another limitation of the current study is that a selection bias may have occurred, since only 20% of the potential study participants agreed to participate in the study. The participating patients were younger and had a more recent stroke. Furthermore, most of the patients had memory complaints and were willing to participate in a memory training program. Only 10-15% of the stroke population in the Netherlands is referred to rehabilitation clinics. In particular, the elderly part of the stroke population is not represented in this study, because these patients often move to nursing homes. We only included patients in the chronic phase after stroke. Therefore, our results should not be generalized to patients in the acute phase after stroke.

This acute phase might be particularly interesting, because coping strategies may change during rehabilitation. Our study population preferred the accommodative strategy of coping, which is in line with results of Brandstädter & Renner (1990), who shows that assimilative coping is dominant in the acute phase, whereas accommodative coping gradually increases in the chronic phase.¹⁵ What will be the best time to start an intervention aimed at improving coping strategy is not yet known. We suggest that it may be best to train effective coping strategies in the acute phase after stroke, because there is more to gain in this phase: more assimilative coping is used, while the use of accommodative coping or the combination of both strategies of coping should be used to positively influence Psychological Health. Thus, training programs aimed at an effective coping strategy early in the rehabilitation phase after stroke may enhance the process of accepting the consequences of stroke, which may help to optimize HR-QoL after stroke. Future intervention studies in stroke patients should investigate whether altering maladaptive coping strategies improves both depressive symptoms and HR-QoL.

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CHAPTER 3

Coping, problem solving, depression, and health-related quality of life in patients receiving outpatient stroke rehabilitation

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Objective

To investigate whether patients with high and low depression scores after stroke use different coping strategies and problem-solving skills and whether these variables are related to psychosocial health-related quality of life (HR-QoL) independent of depression.

Design

Cross-sectional study.

Setting

Two rehabilitation centers.

Participants

Patients participating in outpatient stroke rehabilitation (N=166; mean age, 53.06±10.19 years; 53% men; median time poststroke, 7.29 months).

Interventions

Not applicable.

Main outcome measures

Coping strategy was measured using the Coping Inventory for Stressful Situations; problem-solving skills were measured using the Social Problem Solving Inventory-Revised: Short Form; depression was assessed with the Center for Epidemiologic Studies Depression Scale; and HR-QoL was measured using the five-level EuroQol five-dimensional questionnaire and the Stroke-Specific Quality of Life Scale. Independent samples t tests and multivariable regression analysis, adjusted for patient characteristics, were performed.

Results

Compared with patients with low depression scores, patients with high depression scores used less positive problem orientation ($p=.002$) and emotion-oriented coping ($p<.001$) and more negative problem orientation ($p<.001$) and avoidance style ($p<.001$). Depression score was related to all domains of both general HR-QoL (visual analog scale: $\beta=-.679$; $p<.001$; utility: $\beta=-.009$; $p<.001$), and stroke-specific HR-QoL (physical HR-QoL: $\beta=-.020$; $p=.001$; psychosocial HR-QoL: $\beta=-.054$, $p<.001$; total HR-QoL: $\beta=-.037$; $p<.001$). PPO was independently related to psychosocial HR-QoL ($\beta=.086$; $p=.018$) and total HR-QoL ($\beta=.058$; $p=.031$).

Conclusions

Patients with high depression scores use different coping strategies and problem-solving skills than do patients with low depression scores. Independent of depression, positive problem-solving skills appear to be most significantly related to better HR-QoL.

INTRODUCTION

Living with the consequences of stroke can enormously impact daily life, resulting in diminished health-related quality of life (HR-QoL) in most patients. Utility scores, which range from 0 (death) to 1 (full health), are frequently used to assign value to the level of HR-QoL¹ and are in the range of 0.47 to 0.68 after stroke.^{1,2} HR-QoL after stroke is predicted by several factors including functional constraints, age, sex, socioeconomic status, depression, and coping strategies.²⁻⁶ Particularly, problem-oriented coping strategies are positively associated with HR-QoL.^{7,8} However, patients with stroke may use fewer active, problem-oriented coping strategies.⁹

Depression after stroke has an estimated prevalence of 33%.¹⁰ Depression is also related to other factors such as age, functional limitations, stroke severity, family support, and socioeconomic status.^{11,12} An inverse relation between depression and HR-QoL has been reported.¹³⁻¹⁵ Furthermore, depression is a known effect modifier of the relation between coping strategy and HR-QoL.¹⁶ In a previous study, coping strategy and depression were independently associated with psychological health in patients in the chronic phase after stroke.¹⁷ However, coping strategies may change during rehabilitation.^{18,19} Therefore, we wondered whether the relations between depression, coping, and HR-QoL are also present in patients receiving outpatient rehabilitation treatment.^{18,19}

HR-QoL may also change over time after stroke.^{14,20} Discharge from rehabilitation is a particularly challenging time with respect to HR-QoL. Treatment is completed, and patients are faced with the consequences of stroke in their home environment. This can cause psychological distress and reduced HR-QoL. The ability to use active behavioral coping strategies, such as problem solving, is often helpful during this phase of recovery.⁸

Problem solving and coping are different concepts. Coping is defined as the cognitive and behavioral efforts used to manage specific stressful situations and the emotions they generate,^{21,22} whereas problem solving is defined as "the process of finding solutions to specific problems".^{22(p410)} Problem solving is a coping process, but not all coping processes can be considered problem solving. Problem solving cannot be directly compared with or distinguished from other coping activities because it can serve a variety of coping functions.²² Problem solving is also related to depression and HR-QoL in both population with a disease and healthy population.^{23,24}

Whether coping strategy, problem-solving skills, and depression are independently related to HR-QoL in patients receiving outpatient rehabilitation treatment is unknown. The present study investigated these relations in patients participating in an outpatient stroke rehabilitation program. On the basis of the

findings in a population with chronic stroke,¹⁷ we expected that patients with high depression scores use different coping strategies and problem-solving skills than those with low depression scores and that coping strategies and problem-solving skills are independently related to psychosocial HR-QoL.

METHODS

Study population

Between March 2011 and August 2013, patients in outpatient stroke rehabilitation treatment at Rijndam Rehabilitation Center (the Netherlands) and in Ghent University Hospital (Belgium) were asked to participate. Patients were included if they had been diagnosed with stroke (including subarachnoid hemorrhage) and were aged 18 to 75 years, receiving outpatient rehabilitation treatment for stroke, and able to participate in group therapy. Patients were excluded if they had progressive neurological disorders, life expectancy of ≤ 1 year, insufficient understanding of the Dutch language, subdural hematomas, or moderate or severe aphasia (i.e., score ≤ 20 on the short version of the Token Test²⁵), or partook in excessive drinking or drug abuse. Eligible patients were approached by their rehabilitation physician and invited to participate in an intervention study to evaluate the effectiveness of group training for patients with stroke in addition to the outpatient rehabilitation treatment.²⁶

This was a cross-sectional study of the baseline measurement of a randomized controlled trial examining the effect of problem-solving therapy, in addition to standard treatment, in patients receiving outpatient stroke rehabilitation.²⁶ Outpatient stroke rehabilitation is provided during the postacute phase after stroke for most patients, but it may also be provided for delayed or recurrent stroke effects. The latter group was included in this study because these patients experience comparable problems and may benefit from a problem-solving intervention.

The study was approved by the medical ethics committee of the Erasmus University Medical Center and the ethics committee of Ghent University Hospital. Before the study, written informed consent was obtained from all participants.

Measurement instruments

Patients were assessed by trained research psychologists at the rehabilitation center or at home. HR-QoL was measured using the EuroQol five-dimensional questionnaire (EQ-5D-5L) and the Stroke-Specific Quality of Life Scale (SS-QoL-12). The EQ-5D-5L is a generic questionnaire consisting of 5 questions measured on a 5-point rating scale, which can be combined into 1 utility scale representing the societal perspective of the general public.²⁷ The EQ-5D-5L also includes a visual analog scale in which

patients rate their health on a scale from 0 to 100. The SS-QoL-12 is a disease-specific questionnaire.²⁸ The short version of the questionnaire, which has been validated,²⁹ consists of 12 questions and provides a total score and two subscores: physical and psychosocial HR-QoL. The total and subscores are calculated as the mean scores of the items in the scale (score range, 1-5).

Coping strategy was measured with the Coping Inventory for Stressful Situations (CISS),³⁰ which consists of 48 questions and provides 3 scales, each including 16 items; task-oriented, emotion-oriented, and avoidant coping. Avoidant coping consists of 2 subscales; distraction (8 items) and social diversion (5 items); the remaining 3 items are not used in the subscales. Items are measured on a 5-point rating scale (range, 1-5). The scales and subscales are calculated as the sum of the items belonging to each (sub)scale. Higher scores indicate more use of the coping strategy. The questionnaire has been validated in the Dutch population.³¹

Problem-solving skills were measured using the Social Problem Solving Inventory-Revised: Short Form (SPSI-R:SF). The SPSI-R:SF consists of 10 questions on problem-solving skills in daily situations and contains 5 domains; positive problem orientation (PPO), rational problem solving, negative problem orientation (NPO), impulsivity/carelessness style, and avoidance style. Items are measured on a 5-point rating scale (range, 0-4). Domain scores are calculated as the sum score of the items. The total score is the sum of the items in the positive domains (PPO and rational problem solving) and the reverse score of the items in the negative domains (NPO, impulsivity/carelessness style, avoidance style). Higher domain scores indicate more use of that problem-solving skill, and a higher total score indicates better problem-solving skills in general. The short version is considered reliable and valid.^{32,33}

Depression was measured using the Center for Epidemiologic Studies Depression Scale (CES-D), which consists of 20 items (score range, 0-3). A higher total score indicates more depressive symptoms, and a score of ≥ 16 is considered the cutoff value of the high depression score.³⁴ The score ranges from 0 to 60 and is internally consistent and valid in the Dutch population.³⁵

The short version of the Token Test was used to measure the presence and severity of aphasia. The score ranges from 0 to 36 and has been validated;²⁵ a higher score indicates better performance. A score of ≤ 28 indicates mild aphasic features and ≤ 20 indicates the presence of moderate aphasia; a score ≤ 20 was used as an exclusion criterion for participation in the present study.

The modified Rankin Scale was used to measure the level of independence and as a substitute measure of stroke severity. The scale ranges from 0 (complete independence) to 5 (complete dependence) and is valid in the Dutch population.³⁶

Demographic and clinical information (e.g. side and type of stroke) was obtained from patient records and structured interviews by the research psychologist before

the measurement. Education level was classified in a 7-level system: 1 refers to some years of basic primary education and 7 refers to a university degree or higher.³⁷

Statistical analysis

The sample size required for the randomized controlled trial to detect treatment effects in HR-QoL was 132 patients.²⁶ For this cross-sectional analysis, we used the rule of thumb that at least 10 patients are needed for each determinant in regression models.^{38,39}

Patient characteristics and responses to the questionnaires were evaluated using descriptive statistics. Potential differences between patients with high and low depression scores with regard to patient characteristics, HR-QoL, coping strategies, and problem-solving skills were analyzed using independent samples t tests for continuous variables and chi-square tests for categorical variables.

To assess whether the variables measuring HR-QoL, coping strategy, problem-solving skills, and depression were interrelated, correlation coefficients were calculated and checked for multi-collinearity. Relations between these variables and the following potentially confounding variables was also checked: age, sex, living without a partner, education level (dichotomized into high school or more vs less than high school), time poststroke (dichotomized into ≤ 1 year vs >1 year), side (left vs right), type of stroke (ischemic vs hemorrhagic), aphasia severity, and level of independence (dichotomized into independency [≤ 2] vs dependency [>2]).

To investigate the relative contribution of variables significantly related to at least 1 of the HR-QoL domains ($p < .01$), multivariable regression analyses were performed for each HR-QoL domain. We assumed that HR-QoL could depend on depression score, coping strategy, and problem-solving skills. Variables were entered into the regression model using a blockwise procedure. In block 1, depression score was entered into the model. In block 2, coping was added to the model to estimate its additional value and whether the contribution of depression score on HR-QoL changed. In block 3, problem-solving variables were added to the model. In block 4, potentially confounding variables were added to the model. For each block, the variance explained (R^2 change) and its significance were estimated. P values $< .05$ (2-sided) were considered statistically significant. The model assumptions of normality, linearity, and homoscedasticity were checked.

The analyses were repeated in the patient subgroup within the first year of stroke, excluding patients with delayed stroke effects, to assess whether this altered the results.

Analyses were performed with SPSS version 21.0.

RESULTS

Study population

Of 293 eligible patients approached, 166 provided informed consent. Reasons for nonparticipation were lack of time, logistical problems, or lack of interest. The EQ-5D-5L, SS-QoL-12, SPSI-R:SF, CES-D, and Token Test were completed by all patients, but 1 CISS score was missing. No patient was excluded based on the results of the Token Test.

Table 1 lists the patient characteristics and mean outcome scores. The time poststroke varied (median, 7.29 months; interquartile range, 4.90-10.61 months), but 83.7% were within the first year of stroke. Based on the CES-D cutoff criteria, 39.2% of the study population reported high depression scores. Time poststroke was not related to depression (Table 2).

Patients with and without depression

Several significant differences were found comparing patients with high and low depression scores (see Table 2). Those with high depression scores were younger and more frequently women, living without a partner, and had ischemic stroke. Patients with high depression scores assigned a lower value to all HR-QoL domains, used more emotion-oriented coping strategies, NPO and avoidance style, and used PPO and total positive problem-solving skills less frequently.

Multivariable analysis

Pearson correlation coefficients showed no indication of multi-collinearity. Depression score, emotion-oriented coping, PPO, NPO, avoidance style, age, time poststroke, and modified Rankin Scale score were significantly related to at least 1 HR-QoL domain. These variables were further analyzed using multivariable regression analyses in which the 5 outcomes of generic and disease-specific HR-QoL were entered as dependent variables (Table 3). Sex, living without a partner, education level, side and type of stroke, and severity of aphasia were not related to any HR-QoL domains and were not entered into the regression model.

Regression models were built from 4 blocks of variables. Block 1 showed that the depression score was significantly related to all HR-QoL domains. In block 2, the value of coping strategy was studied in addition to the depression score. Emotion-oriented coping was not independently related to HR-QoL. In block 3, the value of problem-solving skills was analyzed in addition to coping strategy and depression score. PPO was significantly related to psychosocial HR-QoL and total HR-QoL, independent of

Table 1. Descriptive variables at baseline (N=166)

Variable	N	%
Sex (male)	88	53.0
Education level (\geq high school)	58	34.9
Partner (no)	45	27.1
Side of stroke (left)	64	40.3
Type of stroke (ischemic)	119	73.5
Time post-stroke (\leq 1 year)	139	83.7
mRS (dependent)	46	27.7
	Mean	SD
Age (years)	53.06	10.19
Aphasia severity (0-36)*	33.11	2.65
Depression score (0-60)†	15.26	9.86
HR-QoL		
Visual analog scale (0-100)‡	65.67	17.09
Utility (0-1)‡	0.76	0.18
Physical (1-5)§	4.19	0.59
Psychosocial (1-5)§	3.39	0.99
Total (1-5)§	3.79	0.68
Coping strategy¶		
Task-oriented (16-80)	51.98	10.94
Emotion-oriented (16-80)	37.70	11.58
Avoidant (16-80)	38.55	10.88
Social Diversion (5-25)	14.39	5.02
Distraction (8-40)	16.81	5.84
Problem-solving skills¶		
PPO (0-8)	5.33	1.65
RPS (0-8)	4.94	1.53
NPO (0-8)	3.89	2.16
ICS (0-8)	4.04	1.87
AS (0-8)	3.48	1.95
Total (0-40)	22.85	5.67

Abbreviations: AS, avoidance style; ICS, impulsivity/carelessness style; mRS, modified Rankin Scale; NPO, negative problem orientation; PPO, positive problem orientation; RPS, rational problem solving.

* Measured using the Token Test.

† Measured using the CES-D.

‡ Measured using the EQ-5D-5L.

§ Measured using the SS-QoL-12.

¶ Measured using the CISS; norm scores: Task-oriented coping: 60.31 (SD 8.65); Emotion-oriented coping: 38.29 (SD 10.52); Avoidant coping: 45.16 (SD 10.11); Social Diversion: 16.16 (SD 4.25); Distraction: 20.39 (SD 5.98).³¹

¶ Measured using the SPSI-R:SF.

Table 2. Differences between patients with high and low depression scores measured using the CES-D

Variable	Depression Score <16 (N=101)		Depression Score ≥16 (N=65)		p-value
	N	%	N	%	
Sex (male)	63	62.4	25	38.5	0.003
Education level (≥ high school)	41	40.6	17	26.2	0.057
Partner (no)	21	20.8	24	36.9	0.022
Side of stroke (left)	44	47.8	20	37.0	0.205
Type of stroke (ischemic)	66	67.3	53	82.8	0.029
Time poststroke (≤1 year)	89	88.1	50	76.9	0.056
mRS (dependent)*	24	23.8	22	33.8	0.157
	Mean	SD	Mean	SD	p-value
Age	54.72	10.77	50.48	8.70	0.008
Aphasia severity†	33.13	2.65	33.08	2.68	0.903
<i>HR-QoL</i>					
Visual analog scale‡	69.37	16.69	59.98	16.24	<0.001
Utility‡	0.81	0.16	0.68	0.18	<0.001
Physical§	4.33	0.59	3.98	0.53	<0.001
Psychological§	3.86	0.80	2.66	0.78	<0.001
Total§	4.09	0.58	3.32	0.53	<0.001
<i>Coping</i> ¶					
Task-oriented	52.60	11.62	51.00	9.80	0.363
Emotion-oriented	32.26	8.77	46.48	10.12	<0.001
Avoidant	38.76	11.25	38.22	10.36	0.754
Social Diversion	14.56	5.05	14.14	5.00	0.599
Distraction	16.63	5.90	17.09	5.79	0.622
<i>Problem-solving skills</i> ¶					
PPO	5.65	1.44	4.82	1.84	0.002
RPS	5.03	1.51	4.80	1.56	0.346
NPO	3.08	1.81	5.14	2.06	<0.001
ICS	3.87	1.64	4.29	2.17	0.183
AS	2.97	1.76	4.26	1.97	<0.001
Total	24.76	4.77	19.92	5.74	<0.001

Abbreviations: AS, avoidance style; ICS, impulsivity/carelessness style; mRS, modified Rankin Scale; NPO, negative problem orientation; PPO, positive problem orientation; RPS, rational problem solving.

* Measured using the mRS. † Measured using the Token Test. ‡ Measured using the EQ-5D-5L. § Measured using the SS-QoL-12. ¶ Measured using the CISS. ¶ Measured using the SPSI-R:SF.

the depression score and coping strategy. In block 4, all relationships were adjusted for age, time poststroke, and modified Rankin Scale score. These variables did not alter the relationships between depression score, problem-solving skills, and HR-QoL (see Table 3).

The same significant relationships were found in the subgroup of patients within the first year of stroke, except that age and modified Rankin Scale score were not significantly related to the visual analog scale and physical HR-QoL, respectively.

Table 3. Depression, coping and problem solving in relation to HR-QoL: outcomes of the multivariable regression analysis

	Visual Analog Scale ^a		Utility ^a		Physical HR-QoL ^a		Psychosocial HR-QoL ^a		Total HR-QoL ^a	
	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value
Block 1										
Depression score ^t	-.634	<.001	-.008	<.001	-.017	<.001	-.070	<.001	-.044	<.001
R ² change	.140	<.001	.229	<.001	.081	<.001	.486	<.001	.401	<.001
Block 2										
Depression score ^t	-.741	<.001	-.010	<.001	-.022	<.001	-.060	<.001	-.041	<.001
Emotion-oriented coping [§]	.130	.368	.002	.143	.006	.249	-.013	.054	-.003	.498
R ² change	.004	.368	.010	.143	.008	.249	.012	.054	.002	.498
Block 3										
Depression score ^t	-.704	<.001	-.010	<.001	-.021	.001	-.056	<.001	-.039	<.001
Emotion-oriented coping [§]	.108	.494	.002	.307	.006	.311	-.013	.067	-.004	.499
PPOII	1.127	.156	.005	.538	.019	.498	.091	.010	.055	.036
NPOII	.276	.707	.003	.716	.020	.451	.010	.768	.015	.544
ASII	-.066	.929	.005	.511	-.029	.290	-.017	.612	-.023	.361
R ² change	.013	.511	.005	.817	.013	.520	.026	.042	.025	.082
Block 4										
Depression score ^t	-.679	<.001	-.009	<.001	-.020	.001	-.054	<.001	-.037	<.001
Emotion-oriented coping [§]	.066	.674	.001	.396	.003	.540	-.012	.082	-.005	.385
PPOII	1.213	.134	.007	.365	.029	.291	.086	.018	.058	.031
NPOII	.139	.849	.001	.857	.009	.735	.014	.664	.011	.638
ASII	.202	.787	.005	.427	-.013	.603	-.024	.476	-.019	.452
Age	-.140	.265	.001	.341	-.009	.043	.008	.151	.000	.935
Time poststroke (≤ 1 year)	.112	.975	-.040	.215	-.112	.356	.028	.859	-.042	.720
mRS (dependent)	-6.222	.026	-.146	<.001	-.386	<.001	-.116	.347	-.251	.006
R ² change	.038	.071	.143	<.001	.122	<.001	.008	.445	.028	.053
R ² total	.195		.387		.224		.532		.456	

Abbreviations: AS, avoidance style; mRS, modified Rankin Scale; NPO, negative problem orientation; PPO, positive problem orientation.

^a Measured using the EQ-5D-5L. [†] Measured using the SS-QoL-12. [‡] Measured using the CES-D. [§] Measured using the CISS. ^{||} Measured using the SPSI-R:SF. [¶] Measured using the mRS.

DISCUSSION

This study supported the hypothesis that patients with high and low depression scores receiving outpatient stroke rehabilitation use different coping strategies and problem-solving skills. In line with other reports, 39.2% of the patients had high depression scores after stroke. A meta-analysis reported a 30 to 36% prevalence of depression after stroke in general and a prevalence of 36% and 34% for rehabilitation-based studies mainly assessing depression in the mid- and long-term phases after stroke, respectively.¹⁰ In line with other studies, our results show that patients with high depression scores poststroke are younger, more often women, living without a partner, and diagnosed with ischemic stroke.^{40,41} In the present study, patients with high depression scores after stroke assigned lower values to all HR-QoL domains. They also used more emotion-oriented coping, NPO, and avoidance style, and less PPO and total positive problem-solving skills.

Furthermore, coping strategy, problem-solving skills, and depression were related to psychosocial and total HR-QoL based on the SS-QoL-12. The regression models explained 53.2% and 45.6% of the variance for the domains psychosocial and total HR-QoL, respectively. We conclude that these domains are well explained by psychosocial variables.

Depression score had the strongest relationship with HR-QoL. In addition to the depression score, PPO was an independent contributor to psychosocial and total HR-QoL. This indicates that patients with high and low depression scores who are skilled with a PPO, which is a coping process, may experience a better HR-QoL. This implies that training in PPO skills may be useful for all patients with stroke. The inverse relationship between emotion-oriented coping and psychosocial HR-QoL did not reach significance. This coping strategy and the problem-solving skills NPO and avoidance style, were only indirectly related to HR-QoL; this may suggest that patients benefitting most from improving these coping and problem-solving strategies are those with high depression scores after stroke. This is in line with data from a large randomized controlled trial showing that problem-solving therapy had a positive effect on depression.⁴² Future research should further elucidate the effects of improving problem-solving skills in patients with depression and to improve HR-QoL.

With respect to general HR-QoL (measured using the EQ-5D-5L) and the domain of physical HR-QoL (measured using the SS-QoL-12), neither coping strategy nor problem-solving skills made a significant contribution to HR-QoL. This is in agreement with our expectations based on the results of a previous study in patients in the chronic phase after stroke.¹⁷ Compared with the SS-QoL-12, the EQ-5D-5L utilities are

largely based on physical parameters. The utility scores found in our population were relatively high compared with other studies.¹² This difference might be attributed to the fact that our study population was selected from patients actively participating in an outpatient rehabilitation program for stroke, which excluded patients with more severe stroke still being treated in the inpatient rehabilitation clinic.

Study limitations

Some study limitations should be addressed. Most patients in our study population had a right hemisphere stroke. This might be attributed to the fact that patients with language comprehension problems (mostly left hemisphere strokes) were not eligible for the present study. In patients with left hemisphere stroke, the problems of depression may be more pronounced.¹¹ Also, the time poststroke varied. Most patients received postacute outpatient rehabilitation for stroke. In addition, a few patients were referred for outpatient rehabilitation for delayed effects of stroke, explaining the range of times poststroke. Excluding the latter subgroup did not alter the results. This finding underlines the need for early recognition of potential problems in daily life that may occur a considerable time after rehabilitation treatment.

Although we did not measure stroke severity, we did measure level of independence, that is, a functional outcome that may be even more relevant. To assess the predictive value of depression, coping strategy, and problem solving on HR-QoL, a multivariable linear regression analysis was used, which assumed a causal relation between the independent and dependent variables. On the basis of the literature, we assumed that HR-QoL depends on psychosocial variables.¹⁵ However, since we used a cross-sectional study design, it is uncertain whether this assumption holds. This needs to be confirmed in a prospective follow-up study (which is currently in progress). Another limitation is that selection bias may have occurred since 43% of eligible patients declined to participate. Furthermore, only part of the stroke population was referred to rehabilitation centers. Elderly patients with stroke are often discharged to nursing homes (25%)⁴³ and are not represented in this study. Therefore, our results can only be generalized to patients who are treated in an outpatient rehabilitation center after stroke.

CONCLUSIONS

This study supports the hypothesized relationship between coping strategy, depression, and HR-QoL in patients receiving outpatient rehabilitation treatment of stroke, as found earlier in patients in the chronic phase after stroke.¹⁷ Moreover, problem-solving skills had additional value for maintaining better HR-QoL. The domains PPO, NPO, avoidance style, total problem solving, and emotion-oriented coping are strongly associated with depression. Of these, PPO appears to be independently related to HR-QoL. These results suggest that training patients in effective problem-solving skills while participating in outpatient rehabilitation programs after stroke could be beneficial in improving both HR-QoL and symptoms of depression.

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CHAPTER 4

The effectiveness of Problem Solving Therapy for stroke patients: study protocol for a pragmatic randomized controlled trial

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Background

Coping style is one of the determinants of health-related quality of life after stroke. Stroke patients make less use of active problem-oriented coping styles than other brain damaged patients. Coping styles can be influenced by means of intervention. The primary aim of this study is to investigate if Problem Solving Therapy is an effective group intervention for improving coping style and health-related quality of life in stroke patients. The secondary aim is to determine the effect of Problem Solving Therapy on depression, social participation, health care consumption, and to determine the cost-effectiveness of the intervention.

Methods/Design

We strive to include 200 stroke patients in the outpatient phase of rehabilitation treatment, using a multicenter pragmatic randomized controlled trial with one year follow-up. Patients in the intervention group will receive Problem Solving Therapy in addition to the standard rehabilitation program. The intervention will be provided in an open group design, with a continuous flow of patients. Primary outcome measures are coping style and health-related quality of life. Secondary outcome measures are depression, social participation, health care consumption, and the cost-effectiveness of the intervention.

Discussion

We designed our study as close to the implementation in practice as possible, using a pragmatic randomized trial and open group design, to represent a realistic estimate of the effectiveness of the intervention. If effective, Problem Solving Therapy is an inexpensive, deliverable and sustainable group intervention for stroke rehabilitation programs.

Trial registration

Nederlands Trial Register, NTR2509

INTRODUCTION

Stroke is an increasing public health problem in the Netherlands: every year, 41,000 people suffer from stroke and over 3% of the total health care costs are related to the treatment of stroke and its consequences.¹ The mortality rate after stroke is 30% and is likely to decrease, which will cause an increase in morbidity.² Almost 50% of stroke survivors experience consequences in daily life that result in a lowered health-related quality of life (HR-QoL).¹ The World Health Organization Quality of Life (WHOQOL) Group defines quality of life as “individuals’ perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns”.³ HR-QoL refers to the health-related aspects of quality of life. On average, utility scores of HR-QoL after stroke range from 0.47 to 0.68 (a utility score equal to death is 0.0 and full health 1.0), which is substantially lower than the value of a healthy reference population (utility score of 0.93).^{4,5} HR-QoL after stroke is predicted by functional constraints, age, sex, and psychosocial factors, like socioeconomic status, depression, and coping style.^{4,6-8} Functional constraints, age, sex, and socioeconomic status cannot or are difficult to change, but coping style could be targeted. The question then becomes if HR-QoL after stroke could be improved through a coping style intervention. If this is possible, a secondary question would be how such improvement relates to depression, health care consumption, and costs.

A common definition of coping style is someone’s preferred way of dealing with different situations. Several coping styles can be distinguished, such as active, passive, and avoidant coping. Wolters et al. (2010) shows that in traumatic brain-injured (TBI) patients, higher HR-QoL in the long term is predicted by an increase in active problem-focused coping style and a decrease in passive emotion-focused coping style. Unfortunately, in this population of TBI patients the active coping decreases over time, while passive coping increases.⁹ This suggests that if the decrease of active coping can be stopped, there is room for improvement in HR-QoL. Stroke patients make even less use of active, problem-oriented coping styles compared to other brain damaged patients.¹⁰ Furthermore, Darlington et al. (2007) shows that in stroke patients, coping becomes more important in determining HR-QoL over time, while the importance of general functioning decreases.¹¹ This would mean that long term HR-QoL could benefit from improved coping.

Coping styles can be influenced by several interventions. Backhaus et al. (2010) shows that an intervention aimed at changing maladaptive coping styles positively influenced psychosocial functioning of TBI patients.¹² However, HR-QoL was not measured in this study. No research is found that investigated an intervention aimed

at improving HR-QoL through the change of maladaptive coping styles in stroke patients. We therefore set out to investigate whether Problem Solving Therapy (PST), which aims at active problem-focused coping, might improve HR-QoL in stroke patients. PST has been proved effective in other patient populations.^{13,14} In stroke patients, PST has been shown successful for the prevention of post stroke depression.¹⁵ Effects on coping style and HR-QoL have not been investigated yet.

Objectives

The primary aim of this study is to investigate whether PST is an effective group intervention for improving active problem-focused coping style and HR-QoL in stroke patients. The secondary aim is to determine the effect of PST on depression, social participation, health care consumption, and the cost-effectiveness of the intervention. The effectiveness of the therapy will be investigated in an open group design, which has not been used in PST research before. PST will be added to the standard care just before the end of the rehabilitation program, as at this moment a relapse in HR-QoL is frequently observed, when patients cannot rely on their therapists anymore.¹⁶ By teaching patients to actively cope with stressful situations, through adapting and realizing their goals, we expect that patients will use more effective coping styles, which consequently may prevent the relapse in HR-QoL, and possibly increase HR-QoL in the long term. With regard to the secondary aims of this study, we expect the incidence of depression to decrease, social participation to improve, and health care consumption to decrease, resulting in a favorable cost-effectiveness ratio for the intervention.

METHODS/DESIGN

Study design and procedure

The effectiveness of PST for stroke patients will be evaluated in a multicenter pragmatic randomized controlled trial (RCT) with one year follow-up, with the intervention performed in the daily practice of a sub-acute outpatient stroke rehabilitation program. As such, the potential effects of the intervention have a good external validity, which allows us to calculate the cost-effectiveness of the therapy compared with standard care.

The study will be performed in Rijndam Rehabilitation Center in collaboration with Erasmus MC, both in the Netherlands, and in Ghent University Hospital in Belgium. Patients are invited by their rehabilitation physician to participate in the study. Before the start of the study, patients need to sign the informed consent form.

Data will be collected at four time points by one of three research psychologists. T₀ is the baseline measurement, performed within three weeks before the start of the intervention phase. T₁ will be performed within ten days after the intervention phase, T₂ six months and T₃ twelve months after the intervention phase (Figure 1).

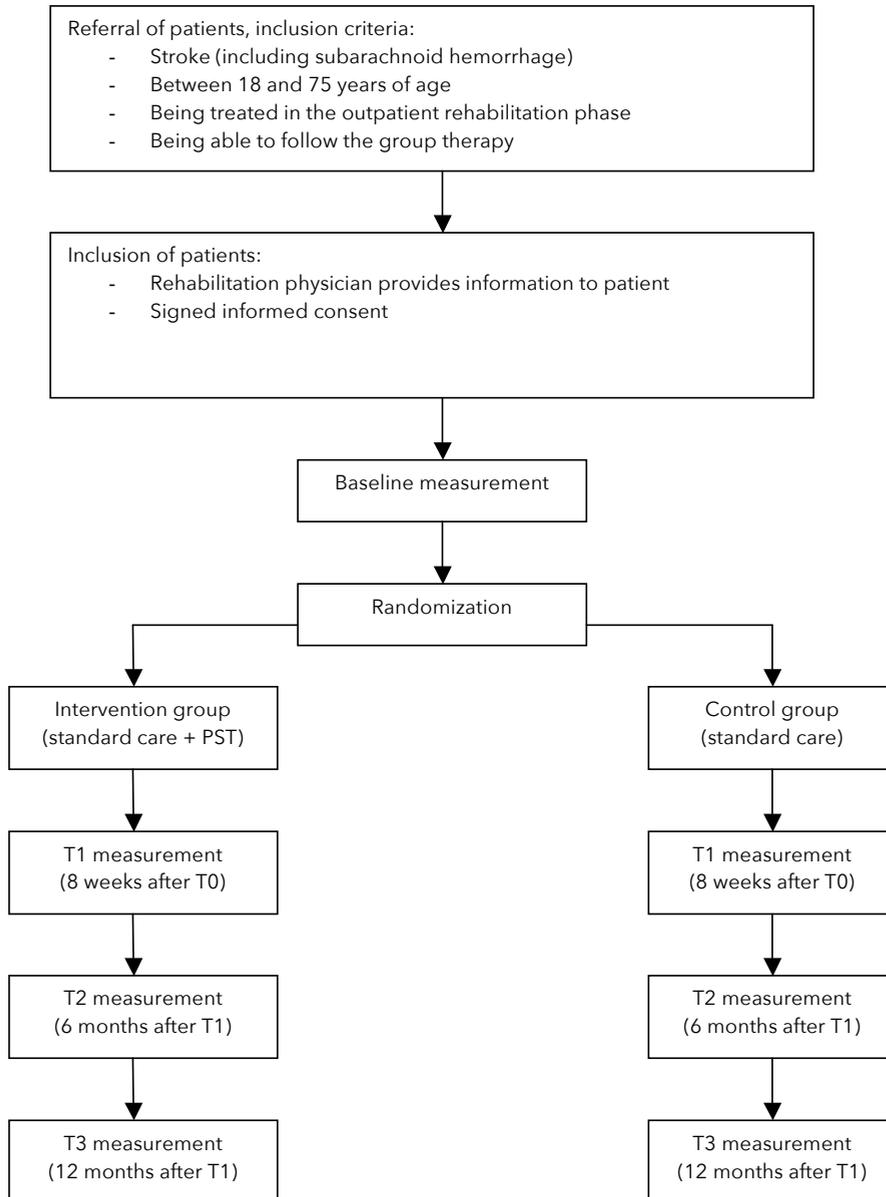


Figure 1. Design of the randomized controlled trial.

The measurements will be performed in the rehabilitation center or at the patients' home in a face-to-face interview. The study has been approved by the Medical Ethics Committee of Erasmus MC University Medical Center and the Ethics Committee of Ghent University Hospital.

Study population

We strive to include 200 stroke patients. Inclusion criteria are: stroke (including subarachnoid hemorrhage), age between 18 and 75 years, being treated in the outpatient rehabilitation phase, and being able to participate in group therapy. Exclusion criteria are: progressive neurological disorders, life expectancy less than one year, insufficient understanding of the Dutch language, excessive drinking or drug abuse, subdural hematomas, moderate and severe aphasia. The same criteria would apply to the implementation of PST in practice, which stresses the pragmatic character of the trial. The inclusion of patients started March 2011 and will end August 2013. The one-year follow-up of all patients will be finished by September 2014.

Randomization

Patients are randomized to the intervention- or control condition using a stratified block randomization procedure with a block size of four. To ensure comparability between the two groups, patients are stratified per rehabilitation center. A member of the research group, who is not involved in the collection of the data, prospectively allocates the patients to the intervention- or control condition in a one-to-one ratio using an online random-number generator. To allow blinded randomization, the allocation information will be put in separate sealed envelopes which are consecutively numbered. At the end of the baseline measurement, the investigator opens the numbered envelop and informs the patient about the condition he or she is assigned to. The research psychologists who perform the baseline and follow-up measurements are blinded for treatment condition. The therapists who provide the intervention are not involved in the collection of the data. The investigator who will analyze the data is not involved in the collection of the follow-up measurements.

Intervention: Problem Solving Therapy

Patients who are assigned to the intervention condition will receive PST in addition to the standard rehabilitation program, which will start during the last eight weeks of outpatient treatment. PST is a widely used and practical intervention method, based on a general model of coping with stress.^{17,18} The model states that having a chronic disease causes stressful daily problems, which increase the chance of experiencing

psychological stress and depressive feelings. Therefore, the aim of PST is to improve the skills to cope with the stressful daily problems in life after stroke.

The intervention will be provided in an open group design, with a continuous flow of patients, which means that patients can enter the group every week and leave the group after eight sessions (Figure 2). The reason for this design is that it studies group therapy in its most feasible form, where patients start and end their programs at different time-points. If we had chosen to study the effect in closed groups, many patients in the similar stage of their programs are necessary. This would only be possible if patients are admitted to large scale rehabilitation centers, which is not the rehabilitation practice in The Netherlands, or patients would have to wait for a long time before entering the group. The open group design has some disadvantages. Patients may feel unsafe when they enter an already existing group. Furthermore, a continuous flow of patients is required to keep a balanced number of patients in the group. Therefore, interventions aimed at rare diseases cannot be studied with an open group design. However, for our population of stroke patients we do expect the design to be suitable and beneficial, because these patients are frequently seen in rehabilitation treatment. An open group design has several benefits as well. Advantages for the patients are that they do not have to wait until they can start with the intervention, they can share their experiences with other 'experienced' stroke patients, and there is room for interaction with many fellow patients. Other advantages are that the intervention is relatively easy to organize and implement in the daily practice of the rehabilitation center. This open group design has not been investigated in PST research yet.

The intervention in this study consists of eight group sessions of 1,5 hours a week, with homework exercises after each session. The group consists of a minimum of three and a maximum of six participants. PST is provided by one to three trained neuropsychologists per rehabilitation center. Solving problems will be structured, by dividing the problem solving process in four steps:

1. Define problem and goal;
2. Generating multiple solutions;
3. Considering the possible consequences of the solutions systematically and select the best solution;
4. Implement the solution and evaluate.

Each session starts with the sharing of experiences from the past week. Then, the model of problem solving will be repeated and explained. If there are some participants who are in the group for a couple of weeks already, they will be asked to explain the model to other new participants. Subsequently, one step of the model

will be highlighted every week. With emphasis on this specific step, the model will be applied to one or more examples from the participants. Finally, the participants will be asked to practice the specific step at home by making a homework assignment. During the sessions, inadequate and irrational thoughts will be challenged by common cognitive interventions. A unique aspect of the intervention is the focus on the definition of the problem in the first step of the model. A clear definition of the problem will lead to a better understanding and more solutions to it.

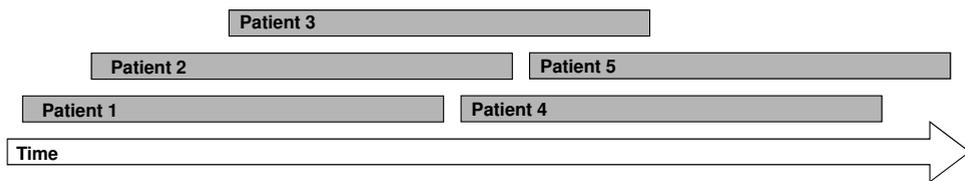


Figure 2. Patient flow in an open group therapy.

Control condition: standard care

Patients who are assigned to the control condition will receive the standard rehabilitation program, in order to be able to study the additional effect of the intervention to the standard rehabilitation program. This standard rehabilitation program consists of individualized amounts of treatment by a physical therapist, occupational therapist, speech therapist, psychologist, social worker, and rehabilitation physician, depending on the severity of stroke. On average, stroke patients in outpatient rehabilitation receive twelve hours of treatment a week during a nine week rehabilitation program.

Outcomes

Primary outcome measures are changes in task-oriented coping and psychosocial HR-QoL in patients in the intervention group in comparison with the control group. Coping style is measured using the Coping Inventory for Stressful Situations (CISS) and the short version of the Social Problem Solving Inventory-Revised (SPSI-R:SF). The CISS questionnaire consists of 48 questions and contains three subscales; Task-oriented coping, Emotion-oriented coping, and Avoidant coping. The subscale Avoidant coping consists of two subscales; Distraction and Social Diversion.^{18,19} Because the PST aims at tasks, 'Task-oriented coping' is chosen as a primary endpoint; the other two subscales are used as secondary endpoints. The SPSI-R:SF questionnaire consists of ten questions about problem solving skills regarding

daily situations. There are five subscales: Positive Problem Orientation, Rational Problem Solving, Negative Problem Orientation, Impulsivity/Carelessness Style, and Avoidance Style, and all are used as secondary endpoints in this trial.²⁰

HR-QoL is measured using the EuroQol (EQ-5D-5L) and the Stroke Specific Quality of Life Scale (SS-QoL-12). The EQ-5D is a generic questionnaire, and consists of five questions regarding mobility, self-care, daily activities, pain/complaints, mood, and a VAS scale. The five dimensions can be combined to one utility scale, representing the societal perspective of the general public.²¹ The SS-QoL-12 is specifically developed for the population of stroke patients.²² We will use the abbreviated version containing twelve items, which has been shown valid.²³ The questionnaire provides a total score and two sub scores: physical and psychosocial, of which the psychosocial subscore is defined as the primary endpoint. The other HR-QoL scores are used as secondary endpoints.

Other secondary outcome measures are differences in depression, social participation, and health care consumption between patients in the intervention and control group. Additionally, the influence of cognitive functioning, personality characteristics, aphasia, type of stroke, side of stroke, level of functioning, and demographic characteristics on the outcomes will be assessed. Finally, the cost-effectiveness of the intervention will be calculated compared with standard care.

Depression is measured using the Center for Epidemiologic Studies Depression Scale (CES-D). This questionnaire consists of twenty items concerning depression, higher scores indicate more depressive symptoms.²⁴

Social participation is measured using the Impact on Participation and Autonomy (IPA). The questionnaire consists of five dimensions; Autonomy indoors, Family role, Autonomy outdoors, Social life and relationships, Work and education.²⁵

Health care consumption is measured using the Trimbos Questionnaire for Costs association with Psychiatric Illness (TiC-P). The questionnaire was developed for economic evaluation in mental health care, and measures health care consumption and productivity losses.²⁶

Sample size calculation

To determine the sample size for measuring differences between the intervention- and control group in coping style and HR-QoL, we searched for comparable effect sizes in the literature. With regard to coping style, there was no data available for this calculation. With regard to HR-QoL, Studenski et al. (2005) measured an increase in HR-QoL after a physical therapy for stroke patients, with a long term effect size f ranging from 0.06 to 0.18.²⁷ Because of the lack of more comparable data, we used

this data and carefully estimated the effect size f to be 0.08. Considering the design of two groups and four repeated measurements, an expected correlation of 0.70, an alpha of 0.05, and a power of 0.80, we calculated a total required sample size of 132 patients based on the F-test. Because potential drop out is estimated at 0.30, we will strive to include 200 patients.

Statistical analyses

Demographic variables will be analyzed with an independent sample T-test for continuous variables, the Mann-Whitney U test for ordinal variables, and the chi-square test for categorical variables. Linear Mixed Models will be used to compare the repeated measurements between treatment groups, taking into account the correlation within and between subjects. We will create models for all the primary and secondary outcome variables, with time, group condition (intervention or control), and the interaction between these variables as predictors. Furthermore, we will control for variables that are accidentally not equally distributed between the two group conditions.

The cost-effectiveness of the intervention will be calculated by counting all the medical and non-medical costs, like productivity losses. The incremental cost-effectiveness ratio will be calculated by dividing the difference in total costs by the difference in quality-adjusted life years (QALYs). These QALYs will be calculated based on the EQ-5D questionnaire. The economic evaluation will be conducted according to the Dutch guidelines²⁸ and includes multivariate probabilistic sensitivity analyses. In the base case scenario the time horizon will be one year. If the effect is still present at one year follow up, a Markov model will be made to model a longer time horizon.

DISCUSSION

This study investigates the effect of PST on coping style and HR-QoL in stroke patients. In addition, the effect on depression, social participation, and health care consumption will be investigated, as well as the cost-effectiveness of the intervention. We will study the effectiveness of PST as close to the implementation in practice as possible, using a pragmatic trial design and an open group therapy. Any pragmatic trial has limitations; MacPherson et al. (2004) argued that a pragmatic trial design cannot be used to determine the specific components of a treatment that caused an effect.²⁹ It may be possible that patients in the intervention group show improvement caused by the extra attention they receive and not so much by the

assumed effective elements of the therapy; this attention effect may be considered a placebo effect. If we would like to distinguish between this 'placebo effect' and the effect of the specific treatment elements, the control group should have received a 'sham therapy'. Such sham therapy would hinder the estimation of the effect of PST in practice, as in practice such additional effort would not take place. Therefore, one of the advantages of the pragmatic study design is that the external validity is better than using a sham-controlled design; the results will be generalizable to the normal rehabilitation setting.³⁰ The study population represents the normal stroke population in the outpatient phase of rehabilitation treatment, and the psychologists will provide the intervention to the patients just as they would do in practice. The results of a pragmatic trial are directly applicable to the usual care setting.³¹ Moreover, if the intervention will prove effective, it will be easy to implement the intervention in the standard rehabilitation program, since it is already in use and the psychologists will already be trained. Other rehabilitation centers can use the therapy manual we developed.

We expect that patients who received PST will use more effective coping styles and experience a higher HR-QoL. Furthermore, we expect that patients after PST will show a decrease in depression score, an increase in social participation, and a decrease in health care consumption, which would lead to a reduction in the health care costs. We expect the intervention to be cost-effective, since the costs of the intervention are relatively low; one psychologist can train three to six patients at the same time. Darlington et al. (2009) estimated the cost-effectiveness of an intervention aimed at coping strategies in stroke patients: the maximum costs for a single patient were 2500 euros, which will be lower if the therapy is provided in a group.³² If PST will be proved effective for stroke patients in outpatient rehabilitation, the intervention will be an inexpensive, deliverable and sustainable group intervention that could be added to usual stroke rehabilitation programs.

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CHAPTER 5

Problem Solving Therapy during outpatient stroke rehabilitation improves coping and HR-QoL: a randomized controlled trial

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Background and Purpose

This study investigated whether Problem Solving Therapy (PST) is an effective group intervention for improving coping strategy and health-related quality of life (HR-QoL) in patients with stroke.

Methods

In this multicenter randomized controlled trial, the intervention group received PST as add-on to standard outpatient rehabilitation, the control group received outpatient rehabilitation only. Measurements were performed at baseline, directly after the intervention, and 6 and 12 months later. Data were analyzed using linear-mixed models. Primary outcomes were task-oriented coping as measured by the Coping Inventory for Stressful Situations (CISS) and psychosocial HR-QoL as measured by the Stroke-Specific Quality of Life Scale. Secondary outcomes were the EuroQol EQ-5D-5L utility score, emotion-oriented and avoidant coping as measured by the CISS, problem-solving skills as measured by the Social Problem Solving Inventory-Revised, and depression as measured by the Center for Epidemiologic Studies Depression Scale.

Results

Included were 166 patients with stroke, mean age 53.06 years (SD, 10.19), 53% men, median time poststroke 7.29 months (interquartile range, 4.90-10.61 months). Six months post-intervention, the PST group showed significant improvement when compared with the control group in task-oriented coping ($p=0.008$), but not stroke-specific psychosocial HR-QoL. Furthermore, avoidant coping ($p=0.039$) and the utility value for general HR-QoL ($p=0.034$) improved more in the PST group than in the control after 6 months.

Conclusions

PST seems to improve task-oriented coping but not disease-specific psychosocial HR-QoL after stroke >6-month follow-up. Furthermore, we found indications that PST may improve generic HR-QoL recovery and avoidant coping.

Clinical Trial Registration-URL

<http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=2509>. Unique identifier: CNTR2509.

INTRODUCTION

After stroke approximately 75% of surviving patients will have problems in mobility, fatigue, emotion, and cognition, measured ≤ 5 years post stroke.¹ Many patients with stroke will also experience reduced health-related quality of life (HR-QoL).² Known predictors of HR-QoL are functional constraints, age, sex, socioeconomic status, depression, and coping strategy.³⁻⁶ Patients with stroke use insufficient active, problem-oriented coping strategies,⁷ whereas active coping strategies are associated with better HR-QoL.^{8,9} During postacute rehabilitation, HR-QoL will increase, along with recovery of bodily functions and activities.¹⁰ After discharge from rehabilitation, a decrease in HR-QoL has been observed,¹⁰ with a further decline in the long term.¹¹ The current study was set up to evaluate whether an add-on module on problem-solving skills in postacute stroke rehabilitation would result in better coping strategies and better HR-QoL.

Problem-solving and coping are different concepts. Coping is defined as the cognitive and behavioral efforts to deal with stressful situations and the emotions they generate,^{12,13} whereas problem-solving refers to "the process of finding solutions to specific problems".¹³ Problem Solving Therapy (PST) is an intervention in which patients are taught to increase structure in solving problems and flexibility by using different coping strategies in various situations. In patients with stroke, PST has been shown successful in reducing symptoms of depression¹⁴ and in preventing poststroke depression¹⁵ although the latter effect was not significant using more conservative analysis. The effects of PST on coping strategy and HR-QoL after stroke are unknown.

The aim of this study was to investigate whether PST, administered as an add-on module in outpatient stroke rehabilitation, is effective in improving coping strategy and HR-QoL after finishing the rehabilitation program. Second, the effect of PST on depression was assessed.

MATERIALS AND METHODS

Design and Participants

In this multicenter, randomized controlled trial, patients were randomly allocated to the PST or control group. Patients were assessed at the rehabilitation center or at home at 4 time points; within 3 weeks before the intervention (T₀), within 10 days post intervention (T₁), and 6 (T₂) and 12 months post intervention (T₃).

Patients at 2 departments of Rijndam Rehabilitation Center (Rotterdam and Dordrecht, the Netherlands) and at Ghent University Hospital (Belgium) were

approached between March 2011 and August 2013. Patients were included if they [1] had suffered a stroke (including subarachnoid hemorrhage), [2] were aged 18 to 75 years, [3] received outpatient stroke rehabilitation treatment, and [4] were able to participate in group therapy. Patients were excluded if they had progressive neurological disorder, life expectancy ≤ 1 year, insufficient understanding of the Dutch language, subdural hematomas, moderate or severe aphasia, or partook in excessive drinking or drug abuse.

The study has been approved by the Medical Ethics Committee of the Erasmus University Medical Center and of Ghent University Hospital. Written informed consent was obtained from all participants.

Procedure

Patients were approached by their physiatrist. Patients willing to participate were invited for the baseline measurement. All assessments and data-entry were performed by trained research psychologists who were blinded for group allocation. All tests were administered in a fixed order during all measurements.

The randomization procedure was performed by an independent investigator using an online random number generator; a random block design (block size of 4) was used stratified for the 3 locations. The allocations were kept in sealed opaque envelopes until the baseline measurement was performed. To start the intervention groups, the first 3 patients per location were directly assigned to the PST group. Thereafter, all patients were randomly assigned to the PST or control group. The flow of new patients with stroke was sufficient to continue the group sessions for most of the time. Eleven times, the PST group was complemented with a patient with traumatic brain injury to secure the minimum number of participants per group ($n=3$). These patients with traumatic brain injury were invited for the PST group only, not for participation in the study.

Intervention: Problem Solving Therapy

Patients assigned to the intervention group received PST as add-on module to standard rehabilitation, during the last 8 weeks of outpatient treatment. PST is a widely used intervention and was slightly adapted for our study; it was provided in an open group design with a continuous flow of patients entering and leaving the group. The PST intervention consisted of 8 group sessions of 1.5 hours a week, with additional homework exercises. Each group consisted of 3 to 6 participants and was provided by a trained neuropsychologist. Solving problems was structured by dividing the problem-solving process in 4 steps: ([1.] Define problem and goal;

[2.] Generate multiple solutions; [3.] Select a solution; [4.] Implement and evaluate). The PST model also focuses on problem orientation, which precedes these steps. In our group therapy, positive problem orientations were encouraged during the interactive problem definition step. A more detailed description of the intervention can be found elsewhere.¹⁶

The control group received standard outpatient rehabilitation only. Standard rehabilitation consisted of pre-defined modules including physiotherapy, occupational therapy, psychology, speech therapy, and social work, which were tailored to individual needs.

Outcome Measures

Coping strategy was measured using the Coping Inventory for Stressful Situations (CISS).¹⁷ This questionnaire consists of 3 scales, each including 16 items, task-oriented, emotion-oriented, and avoidant coping. The items are measured on a 5-point rating scale (range, 1-5). Sum scores are calculated per scale, with higher scores indicating more use of that coping strategy. The questionnaire has been validated in the Netherlands.¹⁸ Task-oriented coping was chosen as primary outcome measure because PST is mainly focused on this coping strategy. Good internal consistency was found (task-oriented: Cronbach's $\alpha > .88$, emotion-oriented: $\alpha > .87$, and avoidant: $\alpha > .82$).

Problem-solving skills were measured with the short version of the Social Problem Solving Inventory-Revised (SPSI-R:SF). This questionnaire consists of 10 questions and contains 5 domains: positive problem orientation (PPO), rational problem solving (RPS), negative problem orientation (NPO), impulsivity/carelessness style (ICS), and avoidance style (AS). The items are measured on a 5-point rating scale (range, 0-4). Domain scores are calculated as sum scores. Higher scores indicate more use of a problem-solving skill. The total score is the sum of the positive domains (PPO and RPS) and the reverse scores of the negative domains (NPO, ICS, AS), a higher total score indicating better general problem-solving skills. The short version is considered reliable and valid.^{19,20} Internal consistency was questionable at To ($\alpha = .68$) and adequate at follow-up ($\alpha > .71$).

HR-QoL was measured using the Stroke-Specific Quality-of-Life Scale (SS-QoL-12) and the EuroQoL EQ-5D-5L. The SS-QoL-12 is a disease-specific questionnaire, specifically measuring problems related to stroke.²¹ The short version contains 12 questions and has been validated.²² It provides 2 subscores; Physical and Psychosocial HR-QoL, calculated as the mean scores of the scale items (score range, 1-5). Psychosocial HR-QoL was chosen as primary outcome measure because PST is

a cognitive rehabilitation intervention. Internal consistency of this scale was good ($\alpha > .80$). The EQ-5D-5L is a generic questionnaire, allowing comparison of HR-QoL between different populations, consisting of 5 items with 5 response categories. These items can be combined into $5^5 = 3125$ health states. For each of these health states, utility scores that range from 0 (death) to 1 (full health) have been established in society. Utilities represent the value of the general public towards the quality of life of different health states.^{23,24} In this way, the societal value of HR-QoL is measured.²⁵ The questionnaire showed adequate internal consistency ($\alpha > .71$).

Depression was measured using the Center for Epidemiologic Studies Depression Scale (CES-D). It consists of 20 items (score range, 0-3). A higher total score (range, 0-60) indicates more depressive symptoms, a score of ≥ 16 is the cutoff value for probable depression.²⁶ The CES-D has been validated in the Netherlands.²⁷ Internal consistency was good ($\alpha > .88$).

Other measures

Personality traits were assessed with the Eysenck Personality Questionnaire Brief Version (EPQ-BV), measuring neuroticism and extraversion. It has been shown internally consistent, reliable and valid.²⁸ Presence and severity of aphasia was measured using the short version of the Token Test.²⁹ Level of independence was measured with the modified Rankin Scale.³⁰ Comorbidity was assessed using the Cumulative Illness Rating Scale (CIRS).³¹ All 4 questionnaires have been validated in the Netherlands.

Clinical and demographic characteristics were obtained from patient records and a structured interview at baseline. Education level was classified using a 7-level system; 1 indicates some years of primary education and 7 a university degree or higher.³²

Sample size calculation

For this trial with 4 repeated measurements, expected correlation of 0.70, α of 0.05, and power of 0.80, we calculated a total required sample size of 132 patients based on the *F*-test, to detect a significant difference in HR-QoL between the 2 groups.¹⁶ We strived to include 200 patients, taking into account potential dropout during the intervention and 1-year follow-up period.

Statistical Analysis

All statistical analyses were performed using SPSS version 21.0 for Microsoft Windows. Potential differences between the PST and control group at baseline were analyzed using independent samples *t* tests for interval variables and chi-square

tests for categorical variables. Differences in changes over time between the groups were analyzed using linear-mixed models, taking into account the correlation within and between subjects. We performed these repeated measurement analyses for each outcome separately. Unstructured covariance structures were used. The outcomes of the 4 measurement times were entered as dependent variables in each model. Fixed factors in the models were group (PST or control) and time point (T₀, T₁, T₂, and T₃), and the interaction between these variables. Each model provided interaction coefficients that represent the mean difference between the groups per time point, using the baseline measurement of the control group as reference. The models were corrected for sex and comorbidity (baseline CIRS score), because these variables accidentally differed between the groups at baseline. $P < 0.05$ were considered statistically significant. Cohen d effect sizes (difference in effect/pooled SD) were calculated.

RESULTS

Study population

Of 293 eligible patients approached, 166 provided informed consent. Reasons for nonparticipation were no time, logistical problems, or lack of interest. The flow of patients through the study is presented in Figure 1. During the intervention period, 4 patients dropped out of the PST group (4.5%). During the 1-year follow-up, another 4 patients dropped out of the PST group and 7 were lost in the control group, resulting in equal dropout rates over the total study time in both groups (9.1% and 9.9%, respectively). The average number of PST-sessions completed was 6.5.

The mean age of the total sample was 53.06 years (SD, 10.19) and 53% were men. The median time poststroke was 7.29 months (interquartile range, 4.90-10.61 months). Left-sided stroke was observed in 40.0% and ischemic stroke in 74.2%. Tables 1 and 2 show the patient characteristics and baseline scores of the outcome variables for the PST and control group.

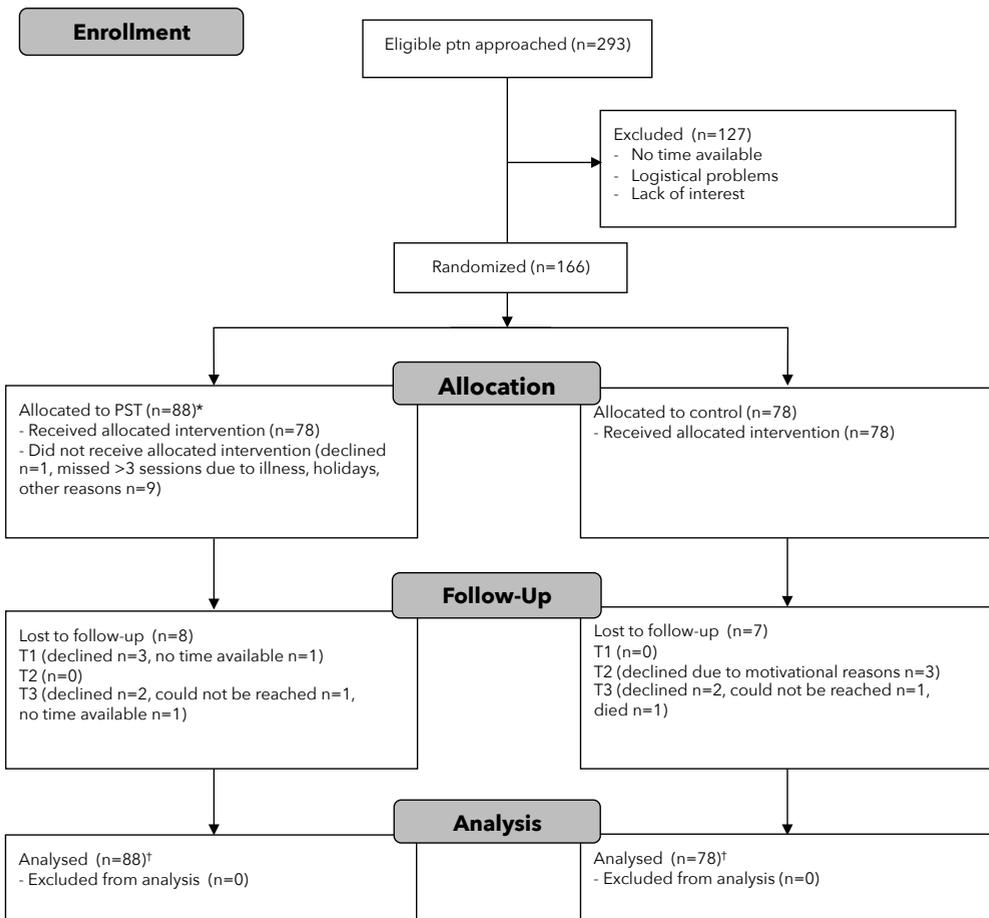


Figure 1. Flowchart of patient inclusion and follow-up

* 9 patients were directly assigned to the PST group, 157 were randomized.

† Analyzed as randomized according to 'intention-to-treat' principle.

Table 1. Patient characteristics of the PST and control group

Variable	PST (n=88)	Control (n=78)	Test Statistic	p-value
Age, years, mean (SD)	52.17 (9.67)	54.07 (10.73)	T(164)=1.203	0.231
Sex, male, n (%)	55 (62.5)	33 (42.3)	X ² (1)=6.768	0.009
Education level, high, n (%)	32 (36.4)	26 (33.3)	X ² (1)=0.167	0.683
Partner, no, n (%)	29 (33.0)	16 (20.5)	X ² (1)=3.239	0.072
Side of stroke, left, n (%)	35 (40.7)	29 (39.2)	X ² (1)=0.117	0.732
Type of stroke, ischemic, n (%)	68 (77.3)	53 (70.7)	X ² (1)=1.819	0.177
Time post stroke, ≤1 year, n (%)	77 (87.5)	62 (79.5)	X ² (1)=1.949	0.163
Modified Rankin Scale score, dependent, n (%)	26 (29.5)	20 (25.6)	X ² (1)=0.315	0.575
Modified Rankin Scale score, mean (SD)	2.11 (.73)	2.00 (.77)	T(164)=-0.971	0.333
Personality (EPQ-BV)				
Extraversion, mean (SD)	7.03 (3.19)	6.23 (2.60)	T(164)=-1.764	0.080
Neuroticism, mean (SD)	4.09 (3.41)	4.09 (3.30)	T(164)=-0.002	0.998
CIRS score, comorbidity, mean (SD)	5.73 (2.67)	6.77 (3.54)	T(164)=2.152	0.033
Aphasia severity, mean (SD)	33.06 (2.76)	33.21 (2.53)	T(164)=0.359	0.720
Currently taking antidepressant medication, n (%)	15 (17.0)	17 (21.8)	X ² (1)=0.599	0.439

CIRS indicates Cumulative Illness Rating Scale, EPQ-BV, Eysenck Personality Questionnaire Brief Version; and PST, problem-solving therapy.

Table 2. Baseline scores of the outcome measures

Variable (Scale Range), Mean (SD)	PST (n=88)	Control (n=78)	Test Statistic	p-value
Coping strategy (CISS)				
Task-oriented (16-80)	51.13 (11.70)	52.92 (10.01)	T(162)=1.042	0.299
Emotion-oriented (16-80)	37.95 (12.08)	37.42 (11.07)	T(160)=-0.291	0.771
Avoidant (16-80)	38.82 (11.68)	38.23 (9.95)	T(163)=-0.343	0.732
Problem-solving skills (SPSI-R:SF)				
Positive problem orientation (0-8)	5.34 (1.63)	5.31 (1.69)	T(164)=-0.129	0.898
Rational problem solving (0-8)	5.11 (1.59)	4.74 (1.45)	T(164)=-1.564	0.120
Negative problem orientation (0-8)	4.03 (2.27)	3.73 (2.03)	T(163)=-0.902	0.368
Impulsivity/carelessness style (0-8)	4.13 (1.97)	3.94 (1.77)	T(163)=-0.651	0.516
Avoidance style (0-8)	3.58 (1.95)	3.36 (1.95)	T(164)=-0.727	0.468
Total score (0-40)	22.70 (5.77)	23.03 (5.59)	T(163)=0.366	0.715
HR-QoL				
SS-QoL: psychosocial (1-5)	3.43 (1.00)	3.34 (0.98)	T(164)=-0.586	0.559
EQ-5D-5L: utility (0-1)	0.74 (0.17)	0.77 (0.18)	T(164)=1.087	0.279
Depression score (0-60)	14.92 (9.41)	15.64 (10.40)	T(164)=0.47	0.640

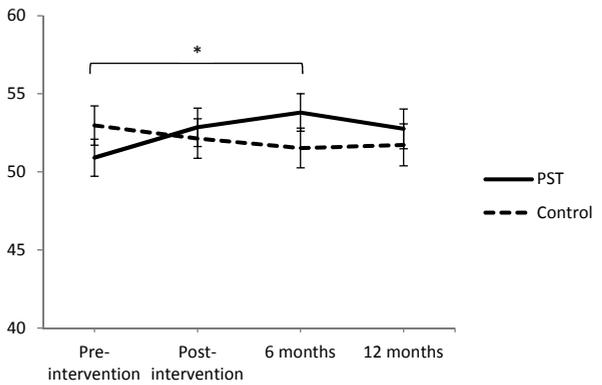
CIRS indicates Coping Inventory for Stressful Situations; HR-QoL, health-related quality of life; SPSI-R:SF, Social Problem Solving Inventory-Revised; and SS-QoL, Stroke-Specific Quality-of-Life Scale.

Effectiveness of PST compared with standard care

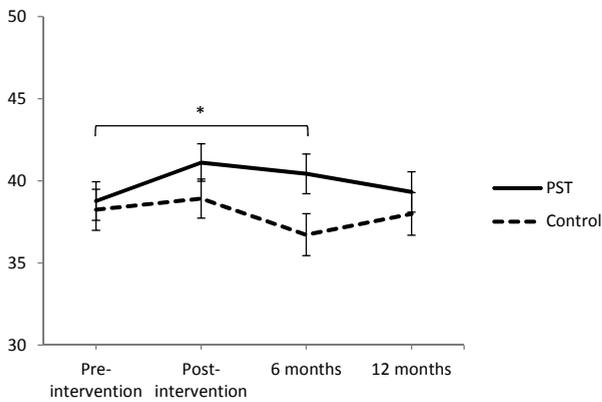
Coping strategy

Figure 2A shows the trajectory of task-oriented coping over the intervention and follow-up time: the primary outcome measure of coping. At 6 months post intervention (T₂), significant differences between the groups were found; the PST group improved significantly more >6-month follow-up than the control group ($p=0.008$; Table 3). The Cohen's d effect size was 0.43. Figure 2A illustrates that the PST group increased in task-oriented coping, whereas the control group slightly decreased. The improvement in task-oriented coping remained stable ≤ 12 months after PST although the difference with standard care only showed a trend towards significance after a year ($p=0.060$). Figure 2B shows a significant difference in the secondary outcome avoidant coping between the PST and control group (effect size, 0.33). The gain in the PST group was not sustained over the 1-year follow-up ($p=0.581$). Emotion-oriented coping decreased over time in both groups ($p=0.004$), but the groups did not differ significantly over time ($p=0.895$).

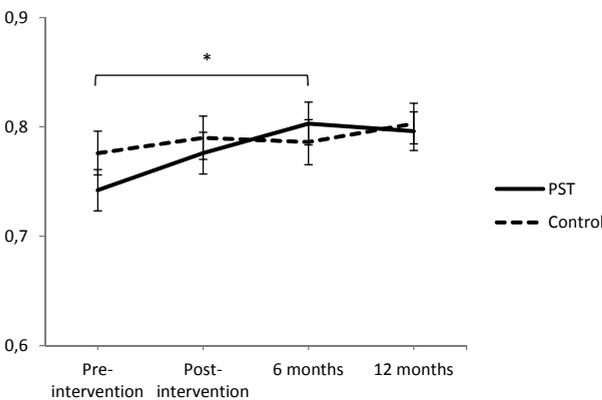
Looking specifically at problem-solving skills, we found no changes over time and no differences between the groups over time (data not shown).



A. Task-oriented coping



B. Avoidant coping



C. Utility score

Figure 2. Effects of PST compared with control group, including standard errors. All analyses were adjusted for sex and baseline comorbidity (CIRS) score. *Significant interaction effect indicating higher scores after PST than control.

Table 3. Effects of PST over time; results of the linear mixed model analyses (N=166)

Variable	T0-T1		T0-T2		T0-T3		Overall
	Mean* (SE)	p-value	Mean* (SE)	p-value	Mean* (SE)	p-value	p-value
<i>Coping</i>							
Task-oriented	2.783 (1.765)	0.117	4.337 (0.622)	0.008	3.095 (1.636)	0.060	0.067
Emotion-oriented	-0.195 (1.469)	0.894	0.692 (1.375)	0.616	0.883 (1.383)	0.524	0.895
Avoidant	1.666 (1.600)	0.299	3.178 (1.524)	0.039	0.808 (1.462)	0.581	0.168
<i>HR-QoL</i>							
SS-QoL:	0.075 (0.134)	0.575	0.063 (0.130)	0.627	-0.047 (0.136)	0.729	0.808
Psychosocial							
EQ-5D-5L: Utility	0.020 (0.026)	0.436	0.052 (0.024)	0.034	0.028 (0.024)	0.245	0.177
Depression	0.568 (1.328)	0.670	-0.938 (1.332)	0.482	1.033 (1.340)	0.460	0.577

HR-QoL indicates health-related quality of life; and SS-QoL, Stroke-Specific Quality-of-Life Scale.

*Mean difference, reference group: control.

Health-Related Quality of Life

The primary outcome psychosocial HR-QoL did not change over the intervention period in any group. Figure 2C shows the course of the secondary outcome utility value of HR-QoL. Over the intervention period, both groups improved equally in general HR-QoL, after which the curves diverged; the PST group continued to increase, whereas the control group leveled off. Six months post intervention (at T2), the increase in utility score significantly differed between the PST and control group ($p=0.034$). The effect size was 0.34. Between 6 and 12 months post intervention, the utility score in the PST group remained stable, whereas the control group caught up, resulting in equal HR-QoL after 12 months ($p=0.245$).

Depression

In both groups, the depression score, a secondary outcome in this study, significantly decreased over the total follow-up time ($p=0.028$). Depression score did not differ significantly between the groups over time ($p=0.577$). The proportion of patients with probable depression decreased from 39.2% at baseline to 32.5% at 1-year follow-up.

DISCUSSION

This study is the first randomized controlled trial assessing the effectiveness of PST, provided as a group intervention during outpatient stroke rehabilitation, on coping strategy and HR-QoL. The results suggest that PST positively affects task-oriented coping skills. The results in terms of HR-QoL recovery are mixed: the primary disease-

specific outcome did not show an effect, whereas the secondary generic outcome did. The expected stagnation in HR-QoL recovery after rehabilitation discharge was observed in the control group, whereas the PST group showed continued improvement of the utility value of HR-QoL until 6 months after PST, suggesting that adding PST to outpatient stroke rehabilitation succeeded in optimizing HR-QoL recovery after discharge.

The finding that stroke-specific psychosocial HR-QoL recovery did not improve while the secondary generic HR-QoL outcome did is remarkable, as one would expect that a disease-specific outcome is more sensitive than a generic. An explanation can be that PST does more than just improving stroke-related HR-QoL problems; newly learned problem-solving skills can be applied in all aspects of life. Another explanation might be a possible measurement issue; we measured psychosocial HR-QoL with the short version of the questionnaire. This version has been validated,²⁰ but may not be sensitive enough to detect small but significant changes.

The effects of PST differed over time; no significant group differences were present directly after the intervention. This may be explained by the fact that both groups received outpatient rehabilitation treatment and were both improving because of the multiple interventions in this standard program. In addition, it may take a while for learning-based interventions to impact psychosocial variables such as coping strategy and HR-QoL. Accordingly, after 6 months, PST resulted in increased use of task-oriented and avoidant coping strategies, indicating an improved flexibility in applying different coping strategies, accompanied by improved utility scores. In the literature, avoidant coping often has been associated with negative outcomes like depression and anxiety. However, a recent study on the psychometric properties of the CISS in patients with acquired brain injury showed that avoidant coping was not related with depression and anxiety, whereas emotion-oriented coping was.³³ We reported the same relationship in our study population in a previous article; avoidant coping was not different between patients with high and low depression scores.³⁴ The result that avoidant coping increased after PST might be explained by the fact that this scale includes many items on social diversion such as seeking company and talking to others, which are encouraged in a group therapy. Being able to apply both task-oriented and avoidant coping strategies in different situations indicates flexibility, which we consider a positive outcome. The effect sizes on coping and utility were rather small and no longer significant after 12 months. This raises the question whether the intervention should be adapted to increase and prolong the effects found. It may be useful to invite participants for more sessions or a refreshment session 6 months post intervention. Future research should assess the effect of such adaptations.

We did not find extra effects of PST on depression, whereas earlier PST studies primarily investigated this outcome.³⁵ Studies in adults with depression presented mixed results; a systematic review³⁶ and a meta-analysis³⁷ both found mixed evidence on effects of PST on depression. In patients with stroke, PST resulted in a lower incidence of depression >12-month follow-up,¹⁵ which disappeared using more conservative analysis. Another study showed a reduction in depressive symptoms ≤12 months.¹⁴ The different results of PST on depression might be because of differences in design, diagnosis, type of PST, type of analysis, or type of control group.³⁷ The studies reporting effects of PST on poststroke depression^{14,15} differed on the study population and used the Hamilton Rating Scale for Depression as outcome measure, which might explain the differences.

This study did show effects on HR-QoL and coping strategy. PST effects on HR-QoL have been investigated in other patient populations. In breast cancer survivors, HR-QoL improved at 12-month follow-up although the PST group was not significantly better than the control group.³⁸ A pilot study investigating telephone-delivered PST (6-week follow-up) found effects in HR-QoL and in active coping, but no control group was included.³⁹ A study investigating a nurse-led telephone-based PST in patients with chronic obstructive pulmonary disease found no differences on problem-oriented coping between the intervention and control group.⁴⁰ These results do not support effects of PST on coping or HR-QoL. In patients with stroke, PST has not been investigated about HR-QoL and coping before. However, other interventions aimed at coping in patients with stroke did find effects.⁴¹ Similar to our intervention, the intervention described by Backhaus et al. (2010) was provided by psychologists, whereas the studies described above without effects on coping were provided by nurses or students. This might point at the importance of a psychologist providing the intervention in order to affect coping.

Unexpectedly, problem-solving skills did not improve after PST, whereas the intervention was specifically aimed at these skills. Maybe PST improves the use of coping strategy in its broad sense, not just problem-solving, supported by the finding that 2 of the 3 coping strategies improved 6 months post intervention. Another explanation is that a measurement issue might have occurred; the questionnaire measuring problem-solving skills might not be sensitive enough because only 2 questions per subscale are used in the short version. The total score of the short version has been validated,^{20,22} but the longer version is more suitable to detect changes in the domain scores. A drawback of the long version might be difficulty in understanding time-consuming questionnaires for stroke patients, especially as part of an extensive test battery.

The intervention was provided in an open group design, which is new in the field of PST research; in earlier PST studies, the groups were closed or PST was provided individually by telephone.³⁵ Our results show that an open group design is feasible and effective in outpatient stroke rehabilitation. The low dropout rate in our study supports this conclusion, as well as the positive feedback we received from patients in the PST group.

A limitation of the study might have been the absence of an active control group intervention. We designed this trial in a pragmatic way because it enables us to observe the added value of PST to standard care. The observed effects cannot be simply explained as an effect of additional attention received by the PST group. The effects were found >6 months post intervention, whereas an effect of additional attention would have been present on the short term only. Furthermore, coping skills are also implicitly trained in standard outpatient rehabilitation, which may decrease the contrast between the intervention and the control group. Another limitation might be the generalizability of the results. Because the intervention has been investigated within the outpatient rehabilitation program, we should be careful in generalizing the results to other settings after stroke. Finally, our population reported a relatively high utility score compared with other stroke populations.^{23,42} The finding that this utility score improved after PST suggests that in populations in which there is more to gain (with lower baseline utility scores), the intervention could even be more beneficial.

SUMMARY

PST seems a useful intervention for patients with stroke, which may have added value to standard outpatient rehabilitation. PST seems to improve task-oriented coping, but not disease-specific psychosocial HR-QoL >6-month follow-up. Furthermore, we found indication that PST may improve generic HR-QoL recovery after stroke and avoidant coping.

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CHAPTER 9

The effectiveness of rehabilitation interventions on health-related quality of life after stroke: a meta-analysis

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Submitted for publication

Objective

Rehabilitation treatment after stroke aims to restore functioning and participation to regain optimal health-related quality of life (HR-QoL). This study synthesized evidence about the effectiveness of stroke rehabilitation interventions, and evaluated which type of intervention is most effective.

Methods

A systematic literature search and meta-analysis included studies if they met the following inclusion criteria: 1) stroke patients; 2) interventions clearly described; 3) SF-36 outcomes reported; 4) controlled/pre-post design; 5) in- or outpatient rehabilitation/community setting. Primary outcomes were the Mental Component Score (MCS) and Physical Component Score (PCS) of the SF-36 at first follow-up. A random-effects meta-analysis was performed on all pre-post studies, and on the subset of controlled studies. Interventions were grouped into multidisciplinary, physical, psycho-social, electrical stimulation/device, and other. PRISMA guidelines and GRADE quality assessment were followed.

Results

32 articles were included, containing 34 intervention and 20 control conditions. In total, 1,744 patients were included, of which 1,072 in the intervention and 672 in the control groups. MCS and PCS significantly improved after intervention (effect size (ES)=0.3, $p<.001$). In the controlled studies MCS improved significantly (ES=0.2, $p=.001$), but PCS did not (ES=0.1, $p=.058$). Little differences were found in effect of different intervention types.

Conclusions

Rehabilitation interventions after stroke are effective in improving HR-QoL on the short-term, most prominently in MCS. There is little evidence to distinguish between intervention types.

INTRODUCTION

Studies describing the effect of stroke rehabilitation interventions on health-related quality of life (HR-QoL) use different designs and show mixed results. For example, several studies investigating physical interventions for stroke, such as exercise of strengthening, with or without a control group report significant improvement in HR-QoL after the intervention,¹⁻⁵ whereas other studies do not report an effect.^{6,7} Therefore, the aim of this study was to synthesize evidence from the literature in order to assess whether stroke rehabilitation interventions improve HR-QoL, and to specify which type of intervention (e.g. multidisciplinary, physical, psycho-social) is most effective. We performed a systematic literature review and meta-analysis to answer these questions.

Most rehabilitation interventions after stroke are goal directed, provided for a relatively short time period and targeted to specific functions or activities. The ultimate goal of rehabilitation is to regain optimal HR-QoL. A generic outcome like HR-QoL is less likely to be sensitive for differences in effectiveness of different rehabilitation interventions than more specific intermediate outcomes like physical functioning. This raises the question whether HR-QoL as a global outcome measure is likely to reflect the effects of rehabilitation interventions targeted to specific goals. Nevertheless, HR-QoL is the ultimate outcome and its generic characteristics allow comparisons between rehabilitation interventions aimed at different intermediate outcomes. For instance, when choosing between psycho-social interventions, electrical stimulation or multidisciplinary rehabilitation, one cannot compare the intermediate outcomes that belong to those interventions: psycho-social functioning, physical function and the combination of both. Comparisons between rehabilitation interventions become possible by choosing HR-QoL as outcome, as HR-QoL is the ultimate goal of rehabilitation.

There are a few meta-analyses about rehabilitation interventions after stroke.⁸⁻¹² These meta-analyses differ regarding both the content of the interventions (e.g. support services, transcranial direct current stimulation, cognitive rehabilitation) as well as the outcomes assessed (social participation, upper extremity impairment, cognitive function, functional recovery). These meta-analyses do not provide results regarding HR-QoL, what prohibits comparison of these different interventions. In the present meta-analysis, we compared the effectiveness of several rehabilitation interventions after stroke, and investigated whether different types of intervention also yield different results.

METHODS

Study selection

Before the start of the review, a review protocol was written, but not published. A systematic literature search was performed to obtain all published articles reporting on the effect of a rehabilitation intervention on HR-QoL in stroke patients. PubMed and Web of Science were searched up to September 2014, using the following search terms: “stroke AND (intervention OR therapy OR training OR treatment OR rehab*) AND (EQ-5D OR EQ5D OR SF-36 OR SF36 OR RAND-36 OR RAND36 OR SF-12 OR SF12 OR SS-QoL OR SSQoL)”.

Inclusion and exclusion criteria

Articles were included in the meta-analysis if they met the following inclusion criteria: 1) patients diagnosed with stroke (total group or identifiable subgroup); 2) clearly described intervention; 3) EuroQoL EQ-5D, Short Form (36) Health Survey (SF-36), SF-12, RAND 36-item Health Survey (RAND-36), or Stroke-Specific Quality-of-Life Scale (SS-QoL) reported (scores available or deductible) before and after the intervention; 4) controlled or pre-post design; 5) in- or outpatient rehabilitation or community setting. Articles were excluded if they reported in another language than English, Dutch, German, or had a sample size smaller than 10.

Two evaluators (MV and LP) independently selected the articles based on title and abstract. The reasons for exclusion were documented. If the two evaluators disagreed on the selection of an article, a third evaluator was consulted, who made the final decision. Full text articles were scrutinized by both evaluators independently. Subsequently, both evaluators independently extracted information from the final set of articles using a standardized data extraction form, based on the CONSORT, STROBE and PRISMA guidelines.¹³⁻¹⁵ Characteristics of the publication, study design, study population, intervention, and outcomes were extracted. If the outcome data was not quantified in the article, the authors were contacted by e-mail and asked for additional data.

Regarding the study design, either experimental or quasi experimental study designs were included, and no restrictions were made on studies without a control group or on type of control group (active control intervention or usual care). With regard to the intervention characteristics no restrictions were made either. Concerning the outcome measures, the SF-36, SF-12, EQ-5D, and SS-QoL were initially included. Most of the included articles used the SF-36 as outcome measure of HR-QoL, while only a few articles used the SS-QoL, EQ-5D, or the SF-12. Because these questionnaires do not provide the same domains, we decided to leave these out of

the meta-analysis and to focus on the outcomes of the SF-36. The questionnaires had to be completed by patients themselves and not by proxies. If HR-QoL was reported for more than one time-point post intervention, the first available follow-up measurement (in most studies performed directly after the intervention) was used.

Types of intervention

The interventions were divided in five subgroups, to estimate the effectiveness of the different types of intervention in improving HR-QoL. The interventions were labeled 'multidisciplinary' (in case of multidisciplinary rehabilitation treatment), 'physical' (only physical intervention), 'psycho-social' (only psycho-social support), 'electrical stimulation/device' (only electrical stimulation or medical device), and 'other' (interventions that do not fit the other categories, like medication). Two evaluators (MV and MH) independently labeled the interventions.

Statistical analysis

The eight domain scores and the mental and physical component scores (MCS and PCS respectively) of the SF-36 were extracted. If these scores were provided in the article (pre-post or pre- and change-scores) these data were used. If only the scores of the eight domains were provided, the MCS and PCS scores were estimated from these domain scores. This was done in three steps: first, the Z scores of the eight subscales were calculated based on the norms for the general U.S. population (total sample).¹⁶ Next, aggregated scores for the physical and mental scores were computed. Finally, these summary scores were transformed into norm-based T-scores (norm: mean 50, SD 10).

In the first meta-analysis, we started with the data of all intervention groups, assessing the differences between pre- and post-treatment scores for the MCS and PCS. Next, we performed subgroup analyses on these scores for the different types of intervention.

In the second meta-analysis, the data from studies that included a control group was analyzed, by assessing the difference in change scores (pre-post treatment) between the intervention and control groups. Next, the difference in change scores was assessed per type of intervention. Finally, for the controlled studies we also evaluated the effect of type of intervention for each of the eight domains of the SF-36 (physical function (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social function (SF), role emotional (RE), and mental health (MH)).

In each meta-analysis, the effects were assessed by pooling the means and SD's of the MCS and PCS (or eight domains) of the separate studies weighted by the

inverse of the sum of the within-study variance for a study plus the between-studies variance, which is standard in a random effects model. We used a random effects model to account for heterogeneity between studies. As a point estimate we used the effect size (ES) Cohen's *d*; an ES of .20 can be considered small, .50 medium and .80 large.¹⁷ An alpha level of .05 was used for statistical significance.

Evaluation of biases and heterogeneity

The quality of the studies included was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) guidelines,¹⁸ which contain five factors of quality: risk of bias, inconsistency of results, indirectness of evidence, imprecision, and publication bias. Two reviewers (MV and MH) independently rated the confidence in estimates of effect (quality of evidence: high, moderate, low, or very low).

The I-squared statistic was used to test heterogeneity. This statistic provides the percentage of the total variability across studies that is due to between study heterogeneity rather than chance.

We checked for the influence of possible confounders on the effect sizes, like sample size, time post stroke, age, sex, duration of intervention, setting, study design. A jackknife analysis was performed, excluding each study one by one from the meta-analysis to evaluate the effect of single studies on the effect sizes and standard errors. Publication bias was assessed by visual inspection of funnel plots and the Egger test. All analyses were performed using Comprehensive Meta Analysis 2.0 (Biostat, Inc.).

RESULTS

Study selection

A total of 387 articles were found in Web of Science and 418 articles were found in PubMed. After removing the duplicate articles, 581 articles were identified (Figure 1). These were evaluated based on title and abstract by two evaluators. For 15 articles a third evaluator was consulted; all 15 articles were excluded.

After evaluation based on title and abstract, 77 articles were reviewed based on their full-text. Of these articles 22 studies were excluded. For six studies additional information was needed to decide whether to in- or exclude these in the meta-analysis. The authors of these articles were contacted by e-mail, a second e-mail was sent if they did not respond to the first request. Four authors did not react or could not be reached, and two authors could not provide the data requested. The 49

remaining articles included four duplicate studies, with follow-up data of the same study population (the first follow-up moment was included).

The remaining 45 articles assessed different types of interventions and contained different HR-QoL questionnaires. 70% of the included articles used the SF-36 as outcome measure of HR-QoL. Only five articles used the SS-QoL, six articles solely used the EQ-5D, and two articles the SF-12. As described in the methods, these 13 articles were left out of the meta-analysis. Finally, 32 articles reporting the outcomes of the SF-36 were included in the meta-analysis. Sixteen studies were published in Europe, six in North America, two in South America, six in Asia, and two in New Zealand.

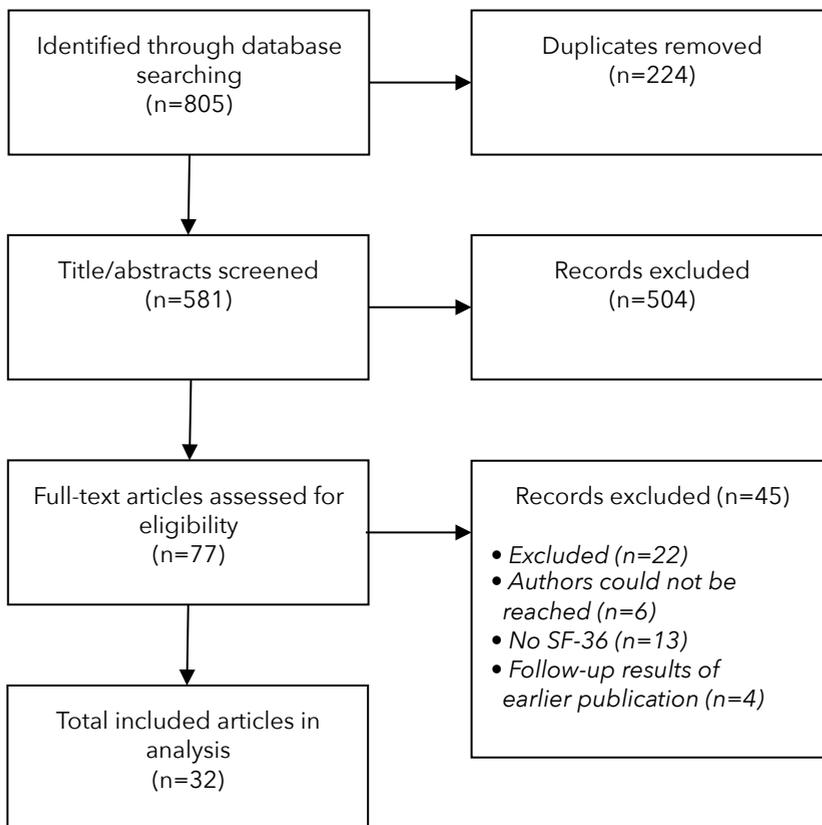


Figure 1. Overview of literature research

Table 1. Descriptive information for studies included in the systematic review

Type of intervention	First author (year)	Sample size (I) Intervention (C) Control	Age, mean (SD)	N male	Time post stroke in days, mean (SD)	Content of intervention (I) and control (C) group
Multi-disciplinary (n=9)	Kirk (2014) ¹⁹	12 (I)	67.5 (11.4)	9	-	(I) Cardiac rehabilitation program
		12(C)	66.8 (7.3)	10		(C) Standard care
	Lund (2012) ²⁰	39 (I)	75 (7.2)	22	-	(I) Lifestyle course + physical activity
		47 (C)	79 (6.5)	20		(C) Physical activity
	Markle-Reid (2011) ²¹	52 (I)	75.8 (12.4)	21	N=30<6 months	(I) Specialized interprofessional team approach
		49 (C)	70.6 (14.5)	24	N=27<6 months	(C) Usual home care
	Lee (2012) ²²	30 (I)	61.27 (13.8)	14	-	(I) Additional inpatient rehabilitation
		22 (C)	63.56 (14.9)	12		(C) Home based care
	Madden (2006) ²³	116 (I)	71.4 (10.4)	57	52.1 (22.6)	(I) Inpatient stroke rehabilitation (C) NA
	O'Connor (2005) ²⁴	50 (I)	55 (47-56) [†]	29	112 (64-183) [†]	(I) Multidisciplinary rehabilitation (C) NA
Bolsche (2002) ²⁵ *	16 (I1)	59.1 (9.26)	8	37.13 (24.86)	(I1) Outpatient rehabilitation	
	18 (I2a)	57.9 (10.04)	5	48.00 (44.57)	(I2 a/b) Inpatient rehabilitation	
	16 (I2b)	59.1 (10.61)	10	31.00 (29.28)	(I2 a/b) Inpatient rehabilitation	
Aprile (2008) ²⁶	66 (I)	66 (10)	42	467 (304)	(I) Multidisciplinary rehabilitation (C) NA	
Lai (2004) ²⁷	21 (I)	69.5 (6.1)	12	1080 (720)	(I) Videoconference intervention (C) NA	
Physical (n=11)	Beinotti (2013) ¹	12 (I)	59	8	2370	(I) Physiotherapy + horseback riding therapy
		12 (C)	52	6	1860	(C) Conventional physiotherapy
	Gordon (2013) ²⁸	64 (I)	63.4 (9.4)	29	384 (108)	(I) Aerobic (walking) training
		64 (C)	64.9 (11.1)	29	354 (108)	(C) Massage affected side

Duration of intervention	Study design	Moment of measurement	Summary of SF36 results
6 weeks	Single-blind RCT	1 months post-stroke, 6 months post-stroke	Intervention group improved on PF and MH
2 hours, 1x/week for 9 months	RCT	Pre- and post treatment	Improvements in both groups, but no difference between groups
12 months	RCT	Pre- and post treatment	Intervention group improved clinically important (but not significant) more on PF and SF
3 months	Controlled, pre-post	Pre- and post treatment	All 8 domains improved in the treatment group, only RP and SF improved in the control group
mean length of stay 48.9 days	Retrospective analysis on 2 combined databases	Pre- and post treatment	PF, VT, SF, MH and PCS improved
-	Observational	Pre- and post treatment	All 8 domains improved, with BP, GH, RE, MH returning to normal levels
38.26 days 30.49 days 30.49 days	Prospective longitudinal	Pre- and post treatment, 6 months follow-up	RP and PF improved in both conditions
50 minutes, 6x/week for 2 months	Observational, prospective	Pre- and post treatment, 2 months follow-up	Improvement in PF and SF at discharge
1.5 hours, 1x/week for 8 weeks	Pre-post	Pre- and post treatment	Improvements on all subscales
16 weeks	Single-blind RCT	Pre- and post treatment	More improvement in the experimental group in the total score and PF, RP, and MH
30 minutes, 3x/week for 12 weeks	RCT	Pre treatment, 6 weeks, post treatment	Trend toward greater improvement for PCS in intervention group

Table 1. Continued

Type of intervention	First author (year)	Sample size (I) Intervention (C) Control	Age, mean (SD)	N male	Time post stroke in days, mean (SD)	Content of intervention (I) and control (C) group
	Holmgren (2010) ²⁹	15 (I) 19 (C)	77.7 (7.6) 79.2 (7.5)	9 12	139.7 (37.3) 126.8 (28.2)	(I) High-intensive exercise program (C) Group discussion
	Olney (2006) ²	37 (I) 35 (C)	63.5 (12.0) 65.8 (11.6)	23 22	1476 (1584) 1224 (1404)	(I) Supervised exercise program (C) Unsupervised home program
	Studenski (2005) ^{3 **}	44 (I) 49 (C)	68.5 (9.0) 70.4 (11.3)	23 27	77.5 (28.7) 74.1 (27.2)	(I) Therapeutic exercise (C) Usual care
	Tibaek (2004) ³⁰	12 (I) 12 (C)	59 (56-72) 62 (52-75) [†]	0 0	360 (60-600) 390 (60-1500) [†]	(I) Pelvic floor muscle training (C) Standard rehabilitation
	Timmermans (2014) ³¹	11 (I) 11 (C)	61.8 (6.8) 56.8 (6.4)	8 8	1022 (1058.5) 1350 (1095)	(I) Robot-assisted arm-hand training (C) Non-robotic arm-hand training
	Kim (2001) ⁶	10 (I) 10 (C)	60.4 (9.5) 61.9 (7.5)	7 7	1764 (1188) 1152 (432)	(I) Maximal isokinetic strengthening (C) Passive range of motion
	Hill (2012) ⁷	10 (I)	46.3 (22-61) [†]	6	2664 (288-7560) [†]	(I) Maximal intensity strength training (C) NA
	Choi (2013) ⁴	10 (I)	48.8 (9.98)	4	297 (51.6)	(I) Wheelchair-based rehabilitation (C) NA
	Padua (2003) ⁵	34 (I)	66 (11.6)	18	1424 (1241)	(I) physical rehabilitation (C) NA
Psycho-social (n=3)	Clarke (2012) ³²	9 (I) 7 (C)	69.00 76.51	6 4	263.4 325.8	(I) Fatigue management group (C) General stroke education
	Claiborne (2006) ³³	16 (I) 12 (C)	70 (13.97) 65 (11.99)	7 10	-	(I) Care coordination model (C) Usual care

Duration of intervention	Study design	Moment of measurement	Summary of SF36 results
7 sessions in 3 days/ week training + 1 hour/week discussion	RCT	Pre- and post treatment, 3 and 6 months follow-up	Benefits in the whole group, no difference between groups
1.5hours, 3x/ week for 10 weeks	RCT	Pre- and post treatment, 6 and 12 months follow-up	PCS increased in the supervised group
36-session, 12-weeks	Single-blind RCT	Pre- and post intervention, 3 months follow-up	Intervention group improved more than usual care on SF
12 weeks	RCT	Pre- and post treatment, 6 months follow-up	No significant differences between the groups
2x30 min, 4x/ week for 8 weeks	RCT	Pre- and post treatment, 6 months follow-up	Improvement in PCS in the control group
45 minutes, 3x/week for 6 weeks	Double-blind controlled pilot study	Pre- and post treatment	No change in either group
9 weeks	Pre-post	Baseline, pre- and post treatment	No change after training
60 minutes, 5x/week for 6 weeks	Pre-post	Pre- and post treatment	Improvements in PF, PR, BP, SR, ER, MH and GH
-	Prospective	Pre- and post treatment, 2-6 months follow-up	PF, GH and PCS improved during rehabilitation
60 minutes, 1x/week for 6 weeks	RCT	Pre- and post treatment, 3 months follow-up	SF improved, but no difference between groups
3 months	Randomized controlled group	Pre- and post treatment	MCS improved in the intervention group

Table 1. Continued

Type of intervention	First author (year)	Sample size (I) Intervention (C) Control	Age, mean (SD)	N male	Time post stroke in days, mean (SD)	Content of intervention (I) and control (C) group
	Brittle (2008) ³⁴	34 (I)	58.8 (53.0-68.3) [†]	18	720 (360-1080) [†]	(I) Conductive education (C) NA
Electrical stimulation/ device (n=4)	Chou (2009) ³⁵	17 (I)	76.29 (9.7)	8	735 (211.8)	(I) Electro-acupuncture
		16 (C)	76.63 (6.5)	8	699 (241.8)	(C) Continued rehabilitation
	Kottink (2010) ³⁶	14 (I)	55.2 (11.36)	10	3265.2 (3344.4)	(I) Implantable nerve stimulator
		15 (C)	52.87 (9.87)	10	2041.2 (1670.4)	(C) Conventional walking device
Fernandes (2006) ³⁷	50 (I)	-	-	-	(I) Functional electric orthosis (C) NA	
Renzenbrink (2004) ³⁸	15 (I)	57.1 (10.4)	8	990 (240-2640) [†]	(I) neuromuscular electrical stimulation (C) NA	
Other (n=5)	Choi-Kwon (2008) ³⁹	76 (I)	58.41 (8.92)	57	327.9 (330.6)	(I) Fluoxetine
		76 (C)	58.18 (8.85)	60	431.1 (249.2)	(C) Placebo
	Hohmann (2009) ⁴⁰	90 (I)	68.2 (9.7)	55	-	(I) Intensified pharmaceutical care
		165 (C)	68.1 (10.8)	107	-	(C) Standard care
	Lindvall (2014) ⁴¹	24 (I)	62.1 (11.4)	12	1496.5 (1387)	(I) Body awareness therapy
		22 (C)	65.6 (9.2)	15	1533 (1642.5)	(C) Continued daily activities
	Shinohara (2012) ⁴²	19 (I)	72.4 (8.7)	9	414 (267)	(I) MOHO-based occupational therapy
17 (C)		75.1 (11.4)	6	651 (234)	(C) Occupational therapy	
Duncan (2011) ⁴³	13 (I)	64 (43-82) [†]	3	1980 (460-5040) [†]	(I) Bowen therapy (C) NA	

Abbreviations: MCS, Mental Component Score; PCS, Physical Component Score; PF, physical function; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social function; RE, role emotional; MH, mental health

*This study contained 3 intervention groups, included as 3 intervention groups in the analyses.

**This study only measured 3 of the 8 domains of the SF-36 and could therefore not be included in the analyses on the MCS/PCS.

[†]Median (interquartile range).

Duration of intervention	Study design	Moment of measurement	Summary of SF36 results
10 group sessions, scheduled daily	Observational, pre-post	Pre- and post treatment	Improvements in MH at $p < .01$ level; RP, RE, SF, VT at $p < .05$ level
20 minutes, 2x/week for 8 weeks	Prospective, randomized, single-blind RCT	Pre- and 8 weeks post treatment 4 weeks before randomization, 26 weeks follow-up	RP, VT, SF, RE, MH, MCS improved Positive effect of the implantable device on the PH, GH and PCS
20 sessions	Pre-post	Pre- and post treatment	All domains improved.
6 hours/day for 6 weeks	Prospective, open label	Implant, explant, 12 and 24 weeks follow-up	All domains, in particular BP, showed improvement in the short term
20mg/day for 3 months	Secondary study of double-blind placebo-controlled trial	Pre- and post treatment, 6 and 12 months follow-up	MH score was higher in the fluoxetine group at 3 months
12 months	Controlled, pre-post	Pre- and post treatment	No change in intervention group, 7/8 domains, MCS and PCS decreased in control group
60 minutes, 1x/week for 8 weeks	Pilot RCT	Pre- and post treatment, 6 week follow-up	No differences in change scores over time between or within the groups
Minimum 20-30 minutes, 2x/week for 3 months	RCT	Pre- and post treatment	The experimental group improved on PF, RP, BP, GH, SF compared to the control group
30-60 minutes, 1x/week for 3 months	Case series	Pre- and post treatment	RP, PCS and total score showed improvements

Data extraction

Of these 32 studies, nine studies reported multidisciplinary rehabilitation treatment (four including a control condition), 11 studies reported a physical intervention (eight including a control condition), three studies reported a psycho-social intervention (two including a control condition), four studies reported electrical stimulation or a medical device (two including a control condition), and five studies reported various interventions (e.g. medication, Bowen therapy), which were grouped in the category 'other' (four including a control condition). The characteristics of the included studies are shown in Table 1.

In one of the extracted articles (Bolsche, 2002) three intervention groups were compared. In that case we included the three intervention groups as separate interventions in the analysis. In another study (Studenski, 2005) only three domains of HR-QoL were included, so that the MCS and PCS could not be calculated. This study was only included in the analysis of the eight subdomains. In total, 33 intervention and 19 control groups were included in the primary analyses of MCS and PCS, and 14 studies were evaluated in the subdomain analysis. The total number of patients was 1,744, of which 1,072 participated in the intervention groups and 672 in the control groups.

Data synthesis

Pre-post effect of interventions on MCS and PCS

The meta-analysis investigating the pre-post effects of all interventions showed that both MCS and PCS significantly improved over the intervention period. The pooled effect size (ES) for MCS was .292 ($n=33$, $p<.001$), the pooled ES for PCS was .265 ($n=33$, $p<.001$).

Pre-post effect by type of intervention

The pre-post effects of the different types of intervention (multidisciplinary, physical, psycho-social, electrical stimulation/device, and other) on MCS and PCS are shown in Figure 2A and 2B respectively. For MCS, all types of intervention resulted in significant improvements ('multidisciplinary' $ES=.267$ ($n=11$, $p=.001$); 'physical' $ES=.169$ ($n=10$, $p=.020$); 'psycho-social' $ES=.563$ ($n=3$, $p=.050$); 'electrical stimulation/device' $ES=.494$ ($n=4$, $p=.007$); 'other' $ES=.246$ ($n=5$, $p=.037$)). PCS significantly improved after 'multidisciplinary' ($ES=.345$, $n=11$, $p=.001$) and 'physical' ($ES=.323$, $n=10$, $p=.001$) interventions, 'electrical stimulation/device' showed a trend towards significance ($ES=.337$, $n=4$, $p=.053$). 'Psycho-social' ($ES=.198$, $n=3$, $p=.134$) and 'other' ($ES=.168$, $n=5$, $p=.105$) interventions did not improve PCS significantly.

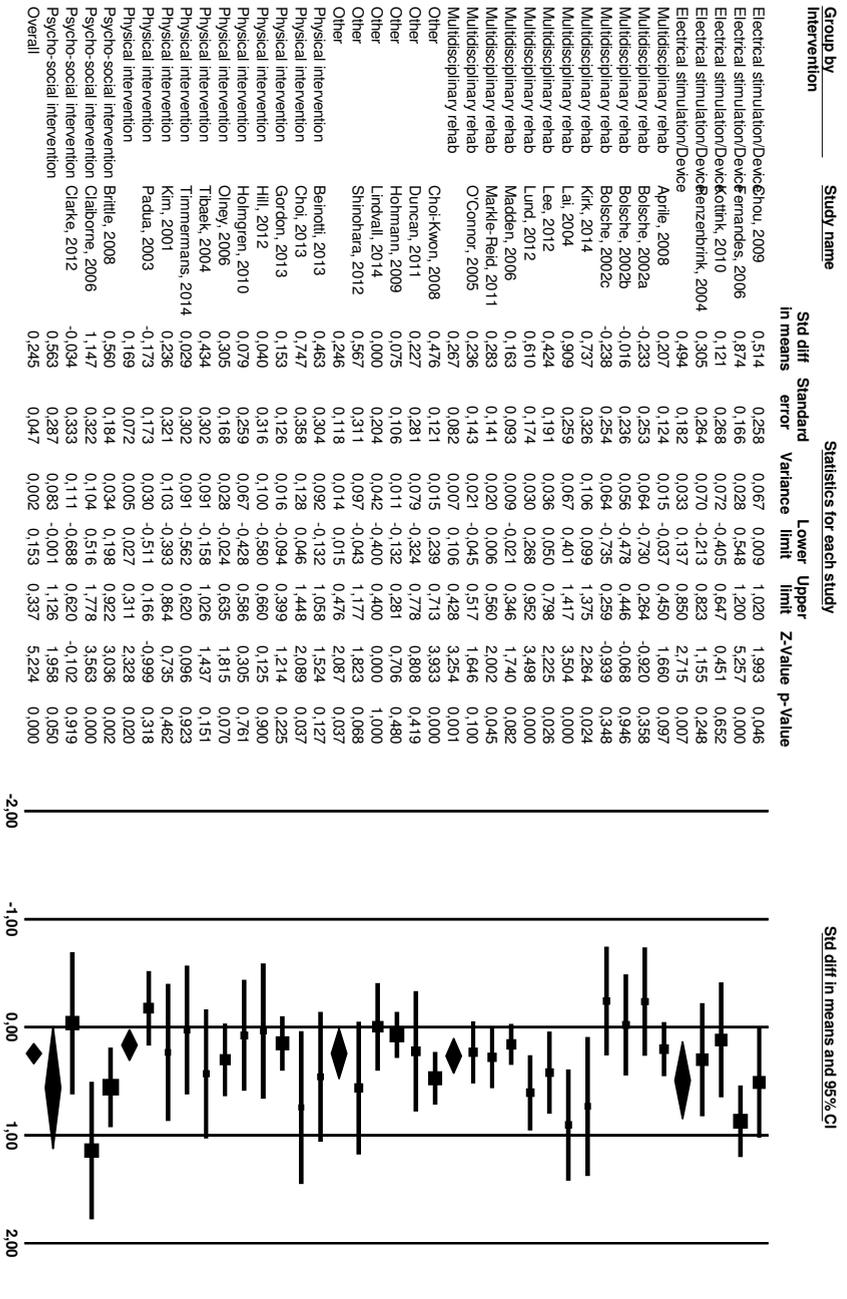


Figure 2. Pre-post scores for MCS and PCS, including pooled ES for different types of intervention

B. PCS

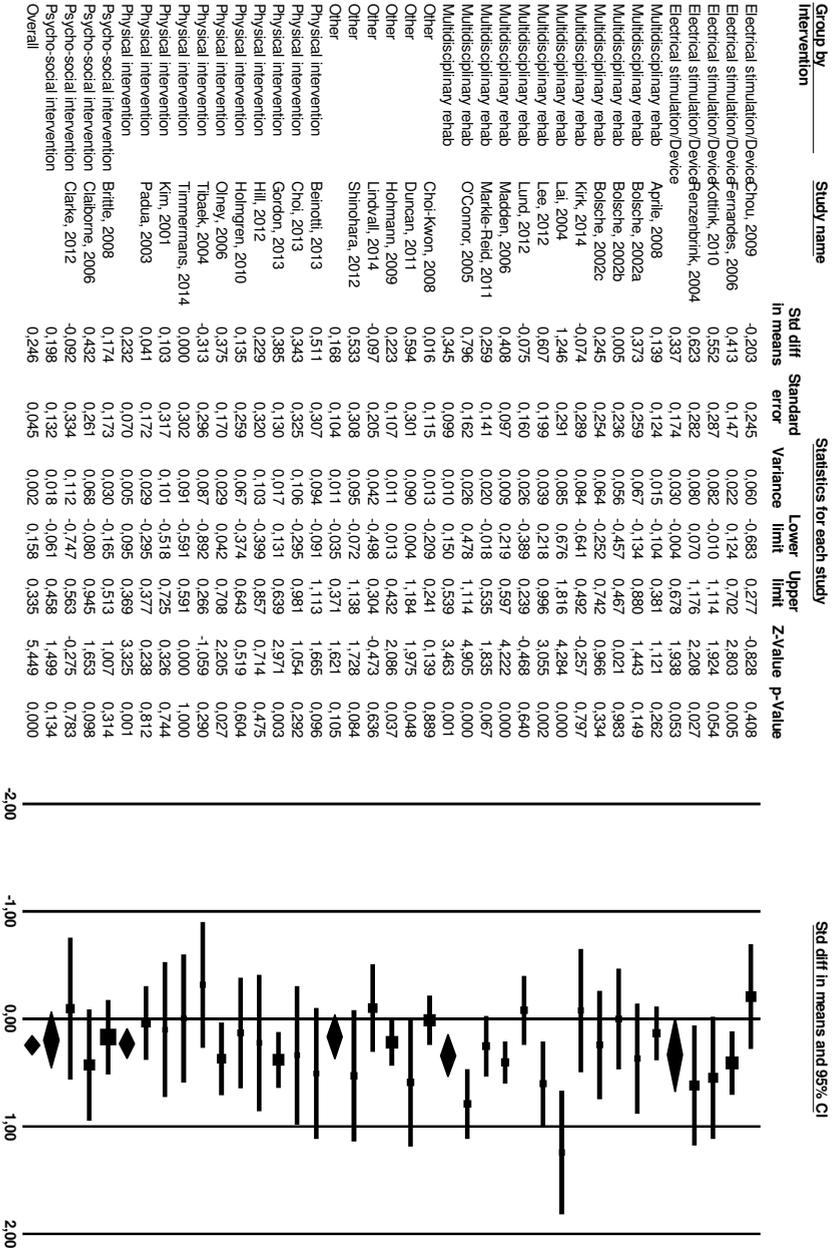


Figure 2. Continued

Controlled effect of interventions on MCS and PCS

The meta-analysis assessing the effect of interventions adjusted for the effect of the control conditions showed that this controlled effect of interventions on MCS was significant with a pooled ES of .242 (n=19, p=.001). The controlled effect of the interventions on PCS was not statistically significant, with a pooled ES of .143 (n=19, p=.058) (Table 2).

Table 2. Effect type of intervention on MCS and PCS (intervention vs control group)

Type intervention	MCS			PCS		
	n	Pooled ES	p-value	n	Pooled ES	p-value
Multidisciplinary	4	.266	.090	4	.112	.372
Physical	7	.028	.799	7	.082	.461
Psycho-social	2	.453	.573	2	.022	.942
Electrical/device	2	.397	.122	2	.457	.519
Other	4	.363	<.001	4	.205	.187
Total	19	.242	.001	19	.143	.058

Controlled effect by type of intervention

Analyzing the controlled effect by different types of intervention showed that MCS significantly improved by 'other' interventions (Table 2). PCS did not significantly change through any type of intervention.

Controlled effects per subdomain of SF-36

Finally, the effect of intervention for each of the 8 subdomains of the SF-36 was evaluated. Table 3 shows that the domains PF, RP, SF, RE, and MH improved significantly more in the intervention groups, compared to the control groups. Differentiating by type of intervention, 'multidisciplinary' interventions significantly improved PF and RE, 'electrical stimulation/device' improved SF and MH, and 'other' improved RP, VT, SF, and MH.

Table 3. Effect of type of intervention on the 8 domains of the SF-36 (intervention vs control)

SF-36 domain	n	Pooled ES	p-value	Type intervention	n	Pooled ES	p-value
Physical Function	14	.270	.007	Multidisciplinary	4	.298	.046
				Physical	4	.499	.073
				Psycho-social	1	-.839	.110
				Electrical/device	2	.598	.104
				Other	3	.206	.325
Role Physical	14	.287	.037	Multidisciplinary	4	.216	.297
				Physical	4	.064	.857
				Psycho-social	1	-.221	.662
				Electrical/device	2	.368	.274
				Other	3	.732	.044
Bodily Pain	13	.089	.211	Multidisciplinary	4	-.044	.819
				Physical	3	-.027	.930
				Psycho-social	1	.070	.889
				Electrical/device	2	.069	.787
				Other	3	.172	.085
General Health	13	.137	.051	Multidisciplinary	4	.160	.199
				Physical	3	.192	.388
				Psycho-social	1	-.287	.571
				Electrical/device	2	.221	.553
				Other	3	.254	.245
Vitality	13	.187	.117	Multidisciplinary	4	.018	.886
				Physical	3	-.097	.822
				Psycho-social	1	-.621	.228
				Electrical/device	2	.915	.056
				Other	3	.244	.014
Social Function	14	.354	.001	Multidisciplinary	4	.310	.104
				Physical	4	.406	.154
				Psycho-social	1	-.759	.146
				Electrical/device	2	.585	.024
				Other	3	.400	.041
Role Emotional	13	.295	.002	Multidisciplinary	4	.310	.013
				Physical	3	-.069	.757
				Psycho-social	1	-.370	.467
				Electrical/device	2	.360	.161
				Other	3	.461	.051
Mental Health	13	.322	<.001	Multidisciplinary	4	.338	.145
				Physical	3	.316	.299
				Psycho-social	1	-.117	.816
				Electrical/device	2	.549	.034
				Other	3	.342	.001

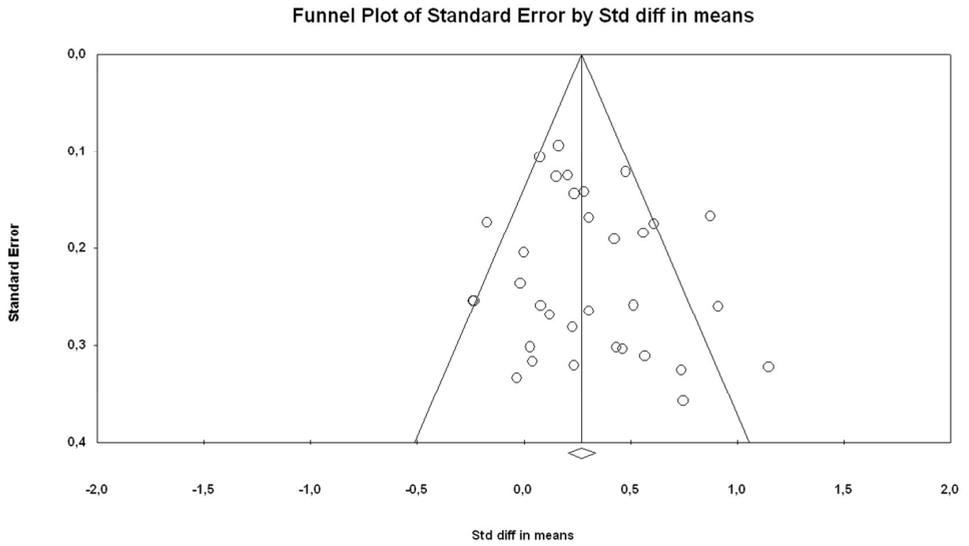
Controlling for/evaluating potential bias

The results of the GRADE quality assessment are shown in Table 4. In the pre-post meta-analyses the risk of bias was serious because no control groups were included. In the meta-analysis of the controlled studies risk of bias was also present because of the lack of blinding of outcome assessors in half of the studies.

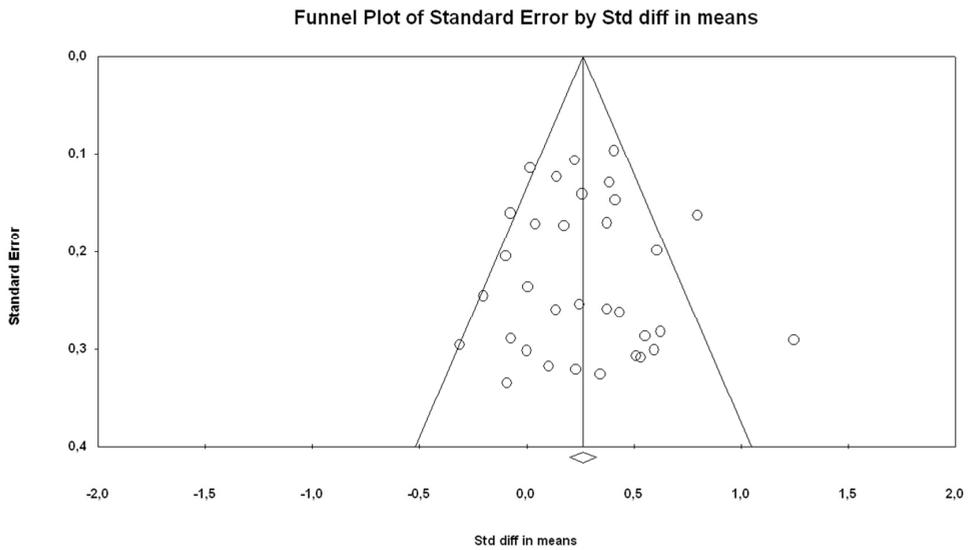
Heterogeneity was present in the pre-post analyses (MCS: $p < .001$; PCS: $p = .001$), but not in the controlled analyses (MCS: $p = .236$; PCS: $p = .135$). Random effects analyses were used in all outcomes to deal with potential heterogeneity. The potential confounders sample size, time post stroke, age, sex, duration of intervention, setting, or study design had no effect on the results. The jackknife analysis showed that none of the single studies affected the effect sizes and standard errors found in the meta-analyses.

The shape of the funnel plots shows no indication for publication bias (Figure 3). The Egger test confirmed that publication bias was not present (MCS: $p = 0.312$; PCS: $p = 0.891$).

The quality of evidence was rated very low for the pre-post studies, based on the absence of control groups and heterogeneity between studies. The evidence based on the controlled studies was rated as moderate quality.



A. MCS



B. PCS

Figure 3. Funnel plots for MCS and PCS

Table 4. GRADE evidence profile: rehabilitation treatment for patients with stroke

Quality assessment				Summary of findings			
Outcome				No of patients			
No of studies (Design)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	(I)	(C)
MCS							
33 (Pre-post)	Serious*	Serious^	No	No	Undetected	1651	0.292 (0.191; 0.394)
19 (RCT)	Serious#	No	No	No	Undetected	559	0.242 (0.104; 0.379)
PCS							
33 (Pre-post)	Serious*	Serious^	No	No	Undetected	1651	0.265 (0.168; 0.362)
19 (RCT)	Serious#	No	No	No	Undetected	559	0.143 (-0.005; 0.291)

Abbreviations: GRADE, Grading of Recommendations Assessment, Development, and Evaluation; MCS, Mental Component Score; PCS, Physical Component Score; RCT, randomized controlled trials; (I), intervention; (C), control; 95% CI, 95% Confidence Interval

#lack of control group

*lack of blinding of participants

^significant heterogeneity

DISCUSSION

This systematic review and meta-analysis showed that stroke rehabilitation interventions are effective in increasing HR-QoL. The pre-post effects on MCS and PCS are comparable ($ES=0.3$) and can be considered small but significant.¹⁷

We were interested in which type of intervention was related to the largest pre-post effects on HR-QoL after stroke. MCS significantly improved by all types of intervention, although the magnitude of the effect size varied. The largest pre-post effect was observed for psycho-social interventions, followed by electrical, multidisciplinary, physical and other interventions. PCS only significantly improved by multidisciplinary and physical interventions. As could be expected, psycho-social interventions affected the mental component of HR-QoL more, while physical interventions affected the physical component more. Psycho-social interventions did not improve the physical component score, while physical interventions did improve the mental component score. Multidisciplinary interventions improved both components of HR-QoL.

After controlling for potential placebo effects or spontaneous recovery, the pooled interventions still showed a significant effect on MCS, whereas the effect on PCS was no longer significant. The effect size of interventions on MCS remained quite stable ($ES=0.2$) compared to the non-controlled analysis, while the number of studies in the meta-analysis decreased (33 to 19). Despite this decrease in power and the comparison with a control group, the stable effect on MCS strengthens our hypothesis that rehabilitation interventions may improve the mental component of HR-QoL. However, we could no longer demonstrate the effectiveness by type of intervention. This is probably due to the small subgroups after removal of uncontrolled studies.

The effect size of the pooled interventions on PCS decreased to 0.1 after adjustment for control groups. We found that most control interventions included some kind of physical therapy (physical activity,²⁰ physiotherapy,¹ massage,²⁸ exercise,² arm-hand training,³¹ range of motion,⁶ walking device,³⁶ or standard care.^{3, 19, 21, 22, 30, 33, 35, 40, 41, 44} Standard care may also have included some kind of physical activity. The lack of contrast between the intervention and control groups regarding physical activity may explain why the effect of rehabilitation interventions on the physical component of HR-QoL diminished after adjustment.

Subgroup analyses on the eight domains of HR-QoL showed that PF, RP, SF, RE, and MH significantly improved after the combined interventions, with varying effect sizes. A remarkable result was observed for MH; psychosocial interventions did not improve this score, while electrical stimulation/device did. However, stratification by

type of intervention and domains of HR-QoL might have resulted in small subgroups which may have precluded finding significant effects on specific domains.

The effects of different clinical interventions on HR-QoL have been reviewed in other patient populations. For example, in a population of patients with multiple sclerosis, a meta-analysis showed that HR-QoL can be improved, and that the effect size varied by type of intervention,⁴⁵ in accordance with our results. The multiple sclerosis meta-analysis included different HR-QoL instruments for which a single index was available, and included only parallel randomized controlled trials. They identified six major types of intervention, and showed the largest effect for 'psychological interventions for mood' (ES=0.7), followed by 'cognitive training' and 'exercise' (ES=0.4), 'medication' (ES=0.3), and 'self-management' and 'complementary and alternative medicine' (ES=0.2), on a single value for HR-QoL. The effect sizes are mostly comparable to those found in our study.

Another example is a meta-analysis in a population of patients with chronic obstructive pulmonary disease.⁴⁶ This systematic review assessed the impact of pulmonary rehabilitation on HR-QoL. They included randomized controlled trials and assessed different interventions and different measures of HR-QoL, not all studies included a measure of HR-QoL. The results of this meta-analysis showed that pulmonary rehabilitation is effective in improving different domains of HR-QoL.

These review studies support our finding that HR-QoL can be improved by various interventions, and that different types of interventions can affect the mental and physical components of HR-QoL differentially.

Limitations

The SF-36 is the most widely used instrument for the measurement of HR-QoL in stroke rehabilitation intervention studies, although other questionnaires are available to measure HR-QoL after stroke.⁴⁷ The number of studies using other instruments was relatively small and therefore these studies were not analyzed. Overall, we found an increase in the summary scores of the SF-36, specifically in the mental score. Our results show that the SF-36 is suitable to detect relevant changes after stroke rehabilitation interventions. This questionnaire evaluates HR-QoL from the perspective of the patient, which is important when evaluating interventions.⁴⁷

Heterogeneity was present in this meta-analysis in the pre-post studies. We used random effects analyses to deal with this and we assessed the effects of potential sources of heterogeneity.

We included different study designs; not all studies contained a control group, and the studies assessed different interventions (regarding content, duration,

intensity, etc.). Because of the heterogeneity between interventions, we grouped the interventions into categories and stratified the analyses by type of intervention. Furthermore, we studied the combined effect of interventions with and without control groups. Without a control group, placebo effects on HR-QoL cannot be ruled out. However including a control condition, which often aims at improved physical functioning, may result in lack of contrast which may diminish effects on specific domains of HR-QoL, notably the physical domains. Therefore, it is important to perform meta-analyses including and excluding studies without control groups.

The time post stroke of the populations in the studies in this meta-analysis varied widely (range: 31 to 3265 days). The studies in the sub-acute phase (mean days post stroke <1 year) are mainly observed in the multidisciplinary intervention group, which seems logical since multidisciplinary rehabilitation treatment is often offered to patients in this phase after stroke. In the chronic phase therapies will be more specifically aimed at the remaining consequences of stroke. We assessed the influence of time post stroke, and found no effect. Regardless of the varying time post stroke, the interventions were successful in improving HR-QoL.

Finally, we only assessed the short-term effects of interventions on HR-QoL. Part of the studies in the analysis provided follow-up scores, but the moments of follow-up differed too much to allow a fair comparison. The effects seemed to remain present in the long term, but future meta-analyses should assess the long-lasting effects of rehabilitation interventions on HR-QoL.

The results of a meta-analysis can be biased by publication bias, which may be present if large studies with large effects are published more often than small studies with small or no effects. We evaluated the presence of publication bias and found no indication in this meta-analysis.

Quality of evidence

In the GRADE approach, randomized controlled trials start as high-quality evidence and observational studies as low-quality evidence. The quality of the studies was adequate regarding most of the quality criteria. Only the blinding of participants was not performed in most studies. This is inherent to the design of non-pharmacological clinical intervention studies, in which blinding is practically impossible. Non-blinding may have resulted in larger effects in the intervention compared to the control groups. Therefore, the quality of evidence was rated down from high to moderate for the controlled studies and from low to very low for the pre-post studies, indicating that we are quite confident in the effect sizes of the controlled studies, but that more research is necessary to confirm our results.

CONCLUSION

Rehabilitation interventions targeted to stroke patients are effective in improving HR-QoL on the short-term. All types of intervention improve the mental component of HR-QoL. Effects on the physical component are found using physical and multi-disciplinary interventions, which disappear by the use of active control therapies.

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General Discussion

CHAPTER 7

Most patients with stroke experience problems in daily life, resulting in a decreased health-related quality of life (HR-QoL).^{1,2} HR-QoL after stroke is predicted by several factors, including functional constraints and psychosocial variables such as depression and coping strategy.^{3,4} Over time, the effect of coping on HR-QoL increases, while the effect of functional constraints decreases.⁴ Immediately after stroke HR-QoL is usually decreased, which increases during post-acute rehabilitation. However, a decline in HR-QoL may re-occur after discharge from rehabilitation, when patients have to deal with the consequences of stroke at home without professional support.⁵ During this phase of recovery, problem solving, a specific coping process, is reported to be helpful by patients with stroke.⁶

Problem Solving Therapy (PST) is an intervention in which patients are taught to increase their skills in flexibly solving problems in various situations. PST has been shown effective in several patient populations.⁷ In patients with stroke, PST has been shown to improve or prevent depression.^{8,9} The effects of PST on coping strategy and HR-QoL after stroke have not been investigated yet. Therefore, the aim of this thesis was [1] to study the relations between coping strategy, problem solving skills, depression and HR-QoL after stroke and [2] to evaluate the effects of PST on coping strategy and HR-QoL in patients with stroke. Finally, we aimed [3] to evaluate the effect of other stroke rehabilitation interventions on HR-QoL. We addressed these aims by conducting two cross-sectional studies, a randomized controlled trial and a meta-analysis.

Concepts of coping and HR-QoL

Coping is commonly defined as the cognitive and behavioral efforts to deal with stressful situations and the emotions they generate.¹⁰ In literature there are several coping theories describing different dimensions of coping. In this thesis we used different coping scales measuring various dimensions of coping: accommodative vs assimilative coping with the Assimilative Accommodative Coping Scale (AACCS),¹¹ and task-oriented, emotion-oriented and avoidant coping with the Coping Inventory for Stressful Situations (CISS).¹² Accommodative coping refers to the adjustment of personal preferences to the situation, while assimilative coping refers to the adjustment of the situation to personal preferences. Task-oriented coping refers to (task-oriented) attempts to solve the problem, cognitive restructuring the problem or changing the situation. Emotion-oriented coping refers to emotional reactions to reduce stress, such as self-blame, becoming angry, becoming tense, or imagining how the situation will develop. Avoidant coping refers to activities to avoid stressful situations by seeking distraction or company. These different dimensions of coping are difficult to compare. In a population of patients with acquired brain

injury, both assimilative and accommodative coping showed positive correlations with task-oriented coping and negative correlations with emotion-oriented coping.¹³ In addition, we measured five dimensions of problem solving: positive problem orientation (PPO), rational problem solving (RPS), negative problem orientation (NPO), impulsivity/careless style (ICS), and avoidance style (AS), measured with the Social Problem Solving Inventory-Revised (SPSI-R:SF).^{14,15} PPO and RPS are considered constructive and adaptive dimensions; PPO refers to the tendency to view problems positively and being optimistic regarding solutions, RPS refers to the systematic use of effective problem-solving techniques. The other three dimensions are considered dysfunctional; NPO refers to a cognitive-emotional set preventing effective problem solving, ICS to the tendency to implement skills impulsively and incomplete, and AS to putting the problem off and waiting for solutions. Problem solving can be considered a coping process, but it cannot be directly compared with or distinguished from other coping dimensions because it can serve a variety of coping functions, depending on the goals and solutions belonging to the problem (e.g. action vs relaxation).¹⁶

HR-QoL is a broad multidimensional construct, including dimensions such as physical functioning, psychological well-being, level of independence, and social well-being. HR-QoL can be measured using generic and disease-specific questionnaires.¹⁷ Generic HR-QoL questionnaires mentioned in this thesis are the Short Form-36 (SF-36)¹⁸ and Euroqol-EQ-5D (EQ-5D-5L).¹⁹ These questionnaires describe health states and allow to focus on subscales but can be used as an index score in economic evaluations as well. This index score is a utility score, representing the societal perspective of the general public.¹⁹ Further, generic questionnaires enable comparison of health states between different patient populations.²⁰ However, these questionnaires may not cover all aspects of HR-QoL typically affected after stroke, such as physical constraints, cognitive impairment or reduced mood. The Stroke-Specific Quality of Life scale (SS-QoL-12) is specifically developed to assess HR-QoL after stroke.²¹ It is recommended to assess HR-QoL using both a generic and disease-specific questionnaire.

MAIN FINDINGS

Coping, problem solving, depression and HR-QoL after stroke

We investigated the relation between coping, depression and HR-QoL after stroke in two cross-sectional studies in the post-acute (**Chapter 3**) and in the chronic phase after stroke (**Chapter 2**). **Chapter 2** describes the relative associations of coping strategy and depression on HR-QoL in patients >18 months after stroke. Coping

strategy and depression score were found to be independently associated with the psychological health dimension of HR-QoL. Patients who prefer an accommodative coping strategy (adjusting personal preferences to the situation) over assimilative coping (adjusting the situation to personal preferences) showed less symptoms of depression and reported higher levels of HR-QoL. Training coping strategies might therefore improve both depression and HR-QoL. If a similar relationship between coping, depression, and HR-QoL exists during the post-acute phase after stroke, this phase may be the best moment to train coping strategies, as in this phase the patient is often participating in a stroke rehabilitation program. Moreover, during post-acute rehabilitation, patients with stroke have been found to use more assimilative coping,¹¹ whereas previous studies suggested that accommodative coping or the combination of both strategies is related to better psychological health.^{4,22} Therefore, we assessed the relation between coping, depression and HR-QoL during post-acute rehabilitation after stroke (median time post stroke 7 months) in **Chapter 3**. In addition, we investigated whether patients with high and low depression scores use different coping strategies and problem solving skills. This study showed that patients with high depression scores used less PPO (a problem solving skill) and emotion-oriented coping and more NPO and AS of problem solving. Independent of depression, positive problem solving skills appear to be most significantly related to better psychosocial and total HR-QoL. These results support a relation between coping strategy, depression and HR-QoL in patients in post-acute outpatient stroke rehabilitation that is similar as in patients in the chronic phase after stroke. We therefore conclude that training coping skills in a post-acute stroke rehabilitation program has the potential to improve both mood and HR-QoL.

Effectiveness of Problem Solving Therapy

We designed a pragmatic randomized controlled trial (RCT) to assess the effectiveness of PST for improving coping strategy, HR-QoL, and depression in patients during outpatient stroke rehabilitation in which we evaluated the effect of PST as an add-on to standard care. This study design allowed for obtaining a realistic estimate of the additional value of PST compared to standard care only. **Chapter 4** describes the details of the design of the RCT and the content of the intervention. Task-oriented coping and stroke-specific psychosocial HR-QoL were chosen as primary outcome measures and depression as secondary outcome measure. The results of the study are presented in **Chapter 5**. PST during post-acute stroke rehabilitation improved task-oriented coping but not disease-specific psychosocial HR-QoL after stroke over six months follow-up. We found indications that PST also improves generic HR-QoL recovery and avoidant coping, but not depression. This suggests that adding PST to

outpatient stroke rehabilitation is effective in optimizing coping skills and HR-QoL recovery after discharge. So, PST as an add-on to a post-acute stroke rehabilitation program prevents a drop in HR-QoL after rehabilitation discharge, which was the primary aim of the study. It is promising that PST, as a relatively short and low cost add-on therapy, shows effect on coping strategy and general HR-QoL at six months follow-up. However, the effects were no longer significant after 12 months, raising the question whether the intervention should be adapted to increase and prolong the effects found.

Which components of the intervention can explain the effects found? The working components of psychotherapeutic interventions are distinguished in specific and common factors.²³ Specific factors refer to the techniques and skills used; in our study the specific ingredients of PST combined with general psychological techniques such as the Socratic dialogue and cognitive behavioral techniques. An important specific aspect of the intervention might be repeating the four steps in the problem solving process multiple times. Common factors include therapeutic alliance, empathy, expectations, therapist effects, and collaboration.²³ Therapeutic alliance is one the most important and well described common factors.²³⁻²⁵ Although PST is highly manualized, the therapeutic alliance is important as well.²⁶ The psychologist has important value in creating a therapeutic alliance, both with herself as a therapist and between members of the group (group cohesion), and in optimizing the group dynamics by observing, supporting, and intervening in these dynamics. The interactive group dynamics should be mentioned as a strong component of the therapy. Modeling, recognition, sharing and peer support are all very strong and positive aspects of group therapy.

The therapist is an important common factor too. Studies investigating the effects of PST on coping and HR-QoL, in which PST was provided by nurses and students, did not show effects.²⁷⁻²⁹ The intervention described in this thesis was provided by psychologists who were specifically trained for providing the PST. However, their basic levels of qualification differed; health-care psychologists and neuropsychologist, both with a master's degree, and psychological assistants with a bachelor degree.

Effectiveness of stroke rehabilitation interventions on HR-QoL

The results of our RCT show that the intervention does affect generic HR-QoL, but not disease-specific HR-QoL, as we hypothesized. This led us to reconsider and discuss the concept of HR-QoL, which is a widely used outcome measure in rehabilitation research. Rehabilitation treatment after stroke often is aimed at specific goals in physical and cognitive functioning to improve social participation and regain

optimal HR-QoL. Many constructs underlie HR-QoL that may or may not be related to the treatment goals of stroke rehabilitation programs. It could be questioned whether HR-QoL is a valid outcome measure for goal specific treatment programs. Studies on efficacy of stroke rehabilitation show mixed results on HR-QoL. Therefore, in **Chapter 6** we performed a systematic literature review and meta-analysis to synthesize evidence to assess whether stroke rehabilitation interventions improve HR-QoL, and to specify which type of intervention is most effective. We aimed to include both disease-specific and generic HR-QoL measures to relate the results to those described in **Chapter 5**. As too little studies in our meta-analysis used disease-specific questionnaires we decided to focus on the SF-36, a generic questionnaire. The results of the meta-analysis show that stroke rehabilitation interventions are effective in improving HR-QoL on the short-term, most prominently in the mental component score. We found little evidence to establish which type of intervention is most effective.

Both the meta-analysis and our RCT show that rehabilitation interventions can improve generic HR-QoL. In our RCT, stroke-specific HR-QoL did not improve. How to explain this result? Patients may apply the newly learned problem solving skills probably in a broader context than just in stroke-related problems. Further, because of time limitations, we used the short version of the stroke-specific HR-QoL questionnaire, which hinders a detailed analysis of the effects on underlying constructs.

SUBJECTIVE EVALUATION OF PST

In our study PST was designed as an open group intervention, meaning that patients could enter and leave the group at different moments in time; ‘experienced’ patients participated in the group together with new members. This is the first study in which PST was offered as an open group therapy. Advantages of this design are that patients do not have to wait until they can start with the intervention, patients can share their experiences with several other patients with stroke, and the group can be implemented in practice relatively easy. Disadvantages may be an unsafe environment within the group, and the need for a continuous flow of patients. The intervention consisted of eight weekly sessions of 1.5 hour provided by a trained psychologist, with three to six participants. The problem solving process was divided in four steps, so that patients would discuss every step in the model twice. The steps in the model are: [1] define problem and goal; [2] generate multiple solutions; [3] select a solution; and [4] implement and evaluate.

We asked patients who participated in the PST group to evaluate the intervention, for which we designed a questionnaire. In this questionnaire patients were asked to grade the intervention, and to answer some multiple choice and open questions. The questions concerned the content of the intervention, the quality of the therapist during the sessions, the group dynamics, the homework assignment forms, and the influence of the intervention on daily life. The questionnaire was filled out by 61% of patients. They evaluated the therapy with a mean 'school grade' of 7.4 on a scale from 0 to 10 (SD=1.0). This Dutch 'school grade' of 7.4 equals an A/A- in the United States. Regarding the content of the intervention, 79.5% of the patients rated the therapy as useful, 77.3% as informative, and 70.5% enjoyed going to the meetings. 93.2% evaluated the quality of the therapist during the sessions positively and 88.6% evaluated the explanations as clear. Regarding the group in which patients participated, 81.8% liked participating in a group, 81.8% evaluated sharing with other patients as helpful, and 84% evaluated the group sessions as pleasant. Regarding the homework assignment forms, 65.1% evaluated the forms as easy to use and 65.9% as useful, 70.4% evaluated the assignments well explained, and 54.6% thought they would use these forms in the future. Regarding the use of the intervention in daily life, 61.4% reported being better at solving problems in daily life, 56.8% reported using the trained skills in daily life, and 43.2% felt more self-confident after the therapy. The duration of the intervention (90 minutes) was rated well by 75%, and 95.5% would recommend the therapy to other patients with stroke.

Regarding the open questions, the answers were quite diverse. Some patients would have wanted more participants in the groups, while other patients evaluated small groups as a positive aspect. Several patients would like more time for sharing experiences and more examples to work with during the sessions. Patients liked recognizing experiences of other patients with stroke, and explicitly liked learning skills to solve problems by themselves.

In summary, the intervention was positively evaluated by the patients who participated in the intervention group. These evaluations are obviously subjective, but the objective low dropout rate in our study supports this conclusion. It confirms that PST would be of additional value to outpatient stroke rehabilitation. The lowest evaluations were given to the homework assignment forms; we might want to adapt these when implementing the therapy in practice. The open group design, which is new in the field of PST research, was evaluated positively, indicating that this design is feasible from the patient perspective. Furthermore, the open group design is easy to implement in practice and the costs are relatively low since the group can be extended to the maximum number of participants any time. When implementing the intervention in practice, one should consider whether the flow of patients is

sufficient and continuous in order to have a sufficient number of participants in this group therapy. If the flow of patients with stroke is insufficient, it is possible to invite patients with other diagnoses, such as traumatic brain injury, to warrant the interactive group dynamics.

METHODOLOGICAL CONSIDERATIONS

Study design

The first two chapters describe cross-sectional studies. In these studies, a multi-variable linear regression analysis and linear mixed model analysis were used. These analyses assume a causal relationship between the independent and dependent variables. Based on the literature, we assumed these relationships are plausible. In order to study the effect of intervention on these relations, we performed the RCT with follow-up measurements over time. Given the positive outcome of our RCT, this causal relationship was supported with empirical evidence.

The randomized controlled trial investigating the effectiveness of PST was designed in a pragmatic way. PST was an add-on therapy and compared to a regular post-acute stroke rehabilitation program without active control therapy. This allows to measure the added value of PST to standard care, which is important for clinical practice. A critical note could be the possible effect of extra attention in the intervention group, but this effect would have been strongest in the short term only, while we found effects six months after the intervention. Further, if we would like to distinguish between the effect of attention and the effect of the specific treatment elements, the control group should have received a control therapy with the same number and duration of sessions, but without psychological intervention. This could decrease the contrast between the intervention and control group. One of the advantages of the pragmatic study design is that the external validity is better than using a sham-controlled design; the results will be generalizable to the normal rehabilitation setting.³⁰

Sampling bias might have been present in the studies described in this thesis. Only patients with stroke in a rehabilitation setting were studied in different phases after stroke. The results of **Chapter 2** were obtained from patients in the chronic phase after stroke rehabilitation. However, in **Chapter 3** similar relationships are shown in a population of patients in the post-acute rehabilitation phase after stroke, indicating that the results can be applied to patients both in the post-acute and chronic phase after stroke.

Outcome measures

Different outcome measures are used in this thesis. For the measurement of coping strategy the AACS¹¹ and the CISS¹² are used. In **Chapter 2**, we used the AACS to measure coping strategy while we used the CISS in **Chapter 3** and **4**. The AACS was already assessed in the first study at the moment we decided to use the CISS for the second study. The reason we chose for the CISS questionnaire was the specific domain structure, which is more in line with the PST intervention compared to the AACS. As a result, we cannot compare the results regarding coping in these two cross-sectional studies directly.

For measuring HR-QoL, the World Health Organization Quality of Life-BREF (WHOQOL-BREF),³¹ SS-QoL-12,²¹ EQ-5D-5L,¹⁹ and the SF-36¹⁸ are used in this thesis. In the study in patients with chronic stroke the WHOQOL-BREF was used. When choosing the measures for the study in patients in outpatient rehabilitation, we wanted to include both a disease-specific and generic HR-QoL questionnaire that also could be used for cost-effectiveness analysis. Since we had to be selective when composing the total test battery because of time limitations, we chose for the short questionnaires SS-QoL-12 and EQ-5D-5L. The meta-analysis described in **Chapter 6** was set up to study multiple HR-QoL questionnaires. However, the SF-36 was exclusively used in the majority of studies, which was the reason why we excluded studies using other questionnaires. It would have been interesting using the SF-36 in our RCT, in order to compare the effects of the PST study in this thesis with the stroke rehabilitation interventions studied in the meta-analysis in **Chapter 6**. This comparison can be estimated using the Cohen's d effect sizes (ES).³² The effect of PST on generic HR-QoL in this thesis shows a significant ES of 0.3. The controlled effects of rehabilitation interventions on the mental and physical component scores of the SF-36 in the meta-analysis are 0.2 and 0.1 respectively. The effects observed in the meta-analysis seem smaller compared to the effect found in our thesis, but the results cannot be compared directly since the EQ-5D does not distinguish between mental and physical components of HR-QoL. Furthermore, most control groups in the meta-analysis consisted of active interventions which might result in smaller differences in effects between the groups.

We chose for short versions of the SPSI-R:SF¹⁵ and the SS-QoL-12,²¹ which appear not to be sensitive enough to detect small changes, described in **Chapter 5**. However, in **Chapter 3** relations between subscales of the SPSI-R:SF and the SS-QoL-12 with HR-QoL are found. The short versions of the questionnaires have been validated^{14,33} and distinguish between subscales in our cross-sectional study. However, these questionnaires may not be able to detect changes over time. Probably the longer

versions would have been more sensitive, but the test battery needed a strict selection because of time limitations.

Depression is an important variable regarding HR-QoL after stroke. In this thesis, we did not find an effect of PST on depression. Earlier PST studies in patients with stroke showed beneficial effects of PST on depression. Robinson et al. (2008) showed that PST resulted in a lower incidence of depression up to 12 months follow-up,⁸ which disappeared using more conservative analysis. Mitchell et al. (2009) showed a reduction in depressive symptoms up to 12 months.⁹ The different results of PST on depression might be due to differences in design, diagnosis, type of PST, type of analysis, or type of control group.³⁴ The studies reporting PST on post stroke depression described above differed in the selection criteria for the study population and used the Hamilton Rating Scale for Depression as outcome measure, which might explain the results.

IMPLICATIONS FOR CLINICAL PRACTICE

PST applied during post-acute outpatient stroke rehabilitation improves coping skills and enhances the recovery of HR-QoL. We aimed to prevent the drop in HR-QoL which is often observed after discharge from stroke rehabilitation; PST succeeded in optimizing HR-QoL recovery after discharge. PST helps patients to cope with problems in daily life, which may result in a reduction of health-care consumption and costs. Therefore, we argue to implement the intervention in clinical practice. The addition of PST in outpatient stroke rehabilitation might replace follow-up treatment after discharge.

When implementing the therapy, the open group design might not always be feasible since a sufficient and continuous number of patients entering the group is needed. In a clinical setting more patients will be available for the group therapy than in a research setting, in which half of the patients are randomized to standard treatment only. In our study, incidentally we allowed patients with traumatic brain injury (TBI) to enter the group if not enough participants with stroke were available. We did not ask these patients to fill in the questionnaires, but observation showed that these patients do experience problems comparable to patients with stroke and may benefit from the intervention. This is supported by the study of Backhaus et al. (2010), describing the effectiveness of an intervention aimed at improving coping skills in a population of patients with brain injury.³⁵ Allowing patients with TBI to join the group might be a solution if implementation of the open group design is hindered by low numbers of eligible stroke patients.

FUTURE PERSPECTIVES

The RCT was designed to study the effectiveness of the PST intervention and to study its cost-effectiveness in the setting of outpatient stroke rehabilitation. This is a relevant question, since more than 3% of the total health-care costs are related to the treatment of stroke and its consequences.¹ Economic evaluations are relevant when considering the reimbursement and implementation of new therapies for patients with stroke. The evaluation should be ideally based on a societal perspective, taking into account all relevant costs (direct and indirect costs). Although PST has been evaluated regarding the cost-effectiveness of the intervention in other patient populations,^{36,37} it has not been assessed in the population of patients with stroke. Therefore, we have planned to assess the cost-effectiveness of additional PST compared with standard outpatient stroke rehabilitation as the next step. We collected data regarding costs of health-care and productivity losses, which can be compared to the gain in HR-QoL described in this thesis. This gain is small but significant. PST enhances the recovery of HR-QoL, which may have resulted in improved social participation and decreased health-care use. The costs of the intervention are relatively low since it is provided as a group intervention. Therefore, we expect the intervention to be cost-effective. We will investigate this in detail in the near future.

GENERAL CONCLUSION

This thesis confirmed the importance of coping strategy for HR-QoL during stroke rehabilitation. Coping strategy and depression are independently related to HR-QoL in patients in both the chronic and rehabilitation phase after stroke. Moreover, problem solving skills appear to have additional value for maintaining better HR-QoL. We have adapted the PST intervention for patients receiving outpatient stroke rehabilitation treatment, and showed that PST improves task-oriented coping and enhances general HR-QoL recovery. In addition, PST seems to improve avoidant coping, indicating an increased flexibility in using different coping strategies. This intervention is a promising addition for outpatient stroke rehabilitation. The meta-analysis studying the effects of various stroke rehabilitation interventions confirms that rehabilitation interventions can improve HR-QoL, mostly regarding the mental component score. Stroke rehabilitation treatment should aim for improving HR-QoL. This thesis shows that this can be achieved using the relatively low cost intervention Problem Solving Therapy.

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Summary

In the introductory **Chapter 1** the impact of stroke is discussed, focusing on the psychosocial variables coping strategy, problem solving skills, depression and health-related quality of life (HR-QoL). Problem Solving Therapy (PST) is introduced and the aims of this thesis are mentioned. These are [1] to study relations between coping strategy, problem solving skills, depression and HR-QoL after stroke and [2] to evaluate the effects of PST on coping and HR-QoL for patients with stroke. Finally, we wanted [3] to evaluate the effect of other stroke rehabilitation interventions on HR-QoL.

The first aim of this thesis is covered in **Chapters 2** and **3**. In **Chapter 2** the relative association of coping strategy and depression with HR-QoL in patients in the chronic phase after stroke is investigated. This cross-sectional study included 213 patients >18 months after stroke. Coping strategy was measured using the Assimilative Accommodative Coping Scale, depression using the Center for Epidemiologic Studies Depression Scale (CES-D), and HR-QoL using the World Health Organization Quality of Life-BREF. The results showed that depression was independently related to all domains of HR-QoL (psychological health, physical health, social relationships, and environment). Accommodative coping and assimilative coping were independently related to the domain psychological health, adjusted for depression and education level. The results indicate that patients who prefer an accommodative coping strategy may show less symptoms of depression. In future studies, preferable coping strategies may be trained in order to improve both depression score and HR-QoL.

In **Chapter 3** the relationship between coping, depression and HR-QoL is studied in the rehabilitation phase after stroke. This cross-sectional study aimed to investigate whether patients with high and low depression scores after stroke use different coping strategies and problem solving skills, and whether these variables are related to psychosocial HR-QoL, independent of depression. Coping strategy was measured using the Coping Inventory for Stressful Situations (CISS), problem-solving skills using the Social Problem Solving Inventory-Revised (SPSI-R:SF), depression using the CES-D, and HR-QoL using the EuroQoL-EQ-5D and the Stroke-Specific Quality of Life Scale (SS-QoL-12). A total of 166 patients participating in outpatient stroke rehabilitation were included. The results showed that patients with high depression scores used less positive problem orientation and emotion-oriented coping and more negative problem orientation and avoidance style compared with patients with low depression scores. Depression score was related to all domains of both general HR-QoL and stroke-specific HR-QoL. Positive problem orientation was

independently related to psychosocial and total HR-QoL. The results in **Chapter 3** suggest that training patients in effective problem solving skills while participating in outpatient rehabilitation programs after stroke could be beneficial in improving both HR-QoL and symptoms of depression.

The second aim of this thesis is covered in **Chapters 4** and **5**. We designed a randomized controlled trial (RCT) to study the effect of Problem Solving Therapy on coping strategy and HR-QoL during outpatient stroke rehabilitation. In **Chapter 4** the study protocol of this pragmatic RCT is presented. The study primarily aims to investigate whether PST is an effective group intervention for improving coping strategy and HR-QoL in patients with stroke. The secondary aim is to determine the effect of PST on depression, social participation and health-care consumption, and to determine the cost-effectiveness of the intervention. The methods and design of the study are described in detail, as well as the rationale and content of the intervention. The intervention group receives PST as add-on to standard outpatient rehabilitation, the control group receives outpatient rehabilitation only. The PST intervention consists of eight group sessions of 1.5 hours a week, with homework exercises after each session. The group sessions include three to six participants, and is provided by a trained neuropsychologist. The problem solving process is structured in four steps: [1] define problem and goal; [2] generate multiple solutions; [3] select a solution; and [4] implement and evaluate. Measurements, including both questionnaires and neuropsychological tests, are performed at baseline, directly after the intervention, and six and twelve months later.

The results of the RCT are described in **Chapter 5**. Coping strategy was measured using the CISS, problem-solving skills using the SPSI-R:SF, depression using the CES-D, and HR-QoL using the EQ-5D and the SS-QoL-12. Patients with stroke were approached at outpatient departments of Rijndam Rehabilitation Center in the Netherlands and Ghent University Hospital in Belgium. In total, 166 patients were included in the study. The results show that six months after the intervention, the PST group showed significant improvement when compared with the control group in task-oriented coping, but not stroke-specific psychosocial HR-QoL. Furthermore, avoidant coping and the utility value for general HR-QoL improved more in the PST group than in the control after six months. The results suggest that PST seems a useful intervention for patients with stroke, which may have additional value to standard outpatient rehabilitation. PST seems to improve task-oriented coping, and indications are found that PST may improve generic HR-QoL recovery and avoidant coping.

The third aim of this thesis is covered in **Chapter 6**. Since we were interested in

optimizing HR-QoL, which is the ultimate outcome measure in rehabilitation, we wondered whether other therapies were able to improve this outcome. We performed a systematic literature review and a meta-analysis to synthesize evidence from literature about the effectiveness of rehabilitation interventions after stroke and to evaluate which type of intervention is most effective in improving HR-QoL. A variety of rehabilitation interventions that were studied in RCT's or pre-post designs was included. Primary outcome measures were the Mental Component Score (MCS) and Physical Component Score (PCS) of the Short Form-36. The literature search resulted in 581 articles. Finally, 32 articles were included. 1,728 patients were included in the pre-post designs and 1,259 in the RCTs. Both MCS and PCS significantly improved over the intervention period. In the RCT studies MCS significantly improved more than the control condition, but PCS did not. Little differences were found in the effects of the different types of intervention. The results suggest that rehabilitation interventions targeted to patients with stroke are effective in improving HR-QoL on the short-term, most prominently in the MCS. There is little evidence to distinguish which type of intervention is most effective.

In **Chapter 7** the main findings of this thesis are discussed. The content of the PST intervention has been evaluated by the patients who participated in the PST group. The positive results of this subjective evaluation are presented and discussed. Finally, methodological considerations, implications for clinical practice and future perspectives are discussed. We conclude that coping strategy and depression are independently related to HR-QoL in patients in both the chronic and rehabilitation phase after stroke. In patients receiving outpatient stroke rehabilitation treatment, PST improves task-oriented coping and enhances general HR-QoL recovery. In addition, PST seems to improve avoidant coping. This intervention seems a promising addition for outpatient stroke rehabilitation. Rehabilitation interventions can improve HR-QoL, which should be aimed for in stroke rehabilitation treatment. This thesis shows that this can be achieved using the relatively low cost intervention Problem Solving Therapy.

Samenvatting

In het inleidende **Hoofdstuk 1** wordt de impact van een cerebrovasculair accident (CVA) besproken, gericht op de psychosociale variabelen coping strategie, probleemoplossende vaardigheden, depressie en gezondheidsgerelateerde kwaliteit van leven (HR-QoL). Problem Solving Therapie (PST) wordt geïntroduceerd en de doelstellingen van dit proefschrift worden beschreven. Deze zijn [1] het onderzoeken van de relaties tussen coping strategie, probleemoplossende vaardigheden, depressie en de HR-QoL na een CVA en [2] het evalueren van de effecten van PST op coping en HR-QoL bij CVA patiënten. Tot slot wilden we [3] het effect van andere revalidatie interventies na CVA op HR-QoL evalueren.

De eerste doelstelling wordt in **Hoofdstuk 2** en **3** van dit proefschrift beschreven. In **Hoofdstuk 2** wordt de relatieve associatie van coping strategie en depressie met HR-QoL bij patiënten in de chronische fase na een CVA onderzocht. Deze cross-sectionele studie omvatte 213 patiënten >18 maanden na een CVA. Coping strategie werd gemeten met de 'Assimilatieve Accommodatieve Coping Schaal' (AACS), depressie met de 'Center for Epidemiologic Studies Depression Scale' (CES-D), en HR-QoL met de 'World Health Organization Quality of Life-BREF'. De resultaten lieten zien dat depressie onafhankelijk was gerelateerd aan alle domeinen van HR-QoL (psychische gezondheid, lichamelijke gezondheid, sociale relaties, en omgeving). Accommodatieve coping en assimilatieve coping waren onafhankelijk gerelateerd aan het domein psychische gezondheid, gecorrigeerd voor depressie en opleidingsniveau. De resultaten laten zien dat patiënten met een accommodatieve coping strategie mogelijk minder symptomen van depressie vertonen. Mogelijk kunnen coping strategieën worden getraind om zowel depressie score als HR-QoL te verbeteren.

In **Hoofdstuk 3** wordt de relatie tussen coping, depressie en HR-QoL bestudeerd in de revalidatie fase na een CVA. Deze cross-sectionele studie had ten doel te onderzoeken of patiënten met hoge en lage depressie scores na een CVA verschillende coping strategieën en probleemoplossende vaardigheden gebruiken, en of deze variabelen gerelateerd zijn aan psychosociale HR-QoL, onafhankelijk van depressie. Coping strategie werd gemeten met de 'Coping Inventory for Stressful Situations' (CISS), probleemoplossende vaardigheden met de 'Social Problem Solving Inventory-Revised' (SPSI-R:SF), depressie met de CES-D, en HR-QoL met EuroQoL-EQ-5D en de 'Stroke-Specific Quality of Life Scale' (SS-QoL-12). In totaal werden 166 patiënten in poliklinische revalidatie na een CVA geïncludeerd in deze studie. De resultaten lieten zien dat patiënten met hoge depressie scores minder positieve probleemoriëntatie en emotiegerichte coping gebruiken en meer negatieve probleemoriëntatie en vermijdende stijl van probleemoplossen vergeleken met de patiënten met lage depressie scores. Depressie score was

gerelateerd aan alle domeinen van zowel generieke als CVA-specifieke HR-QoL. Positieve probleemoriëntatie was onafhankelijk gerelateerd aan psychosociale en totale HR-QoL. De resultaten in **Hoofdstuk 3** suggereren dat het trainen van effectieve probleemoplossende vaardigheden in patiënten tijdens het poliklinische revalidatie programma na een CVA kan helpen bij het verbeteren van zowel HR-QoL als symptomen van depressie.

De tweede doelstelling van dit proefschrift wordt besproken in **Hoofdstuk 4** en **5**. We hebben een gerandomiseerde gecontroleerde trial (RCT) uitgevoerd om het effect van PST op coping strategie en HR-QoL tijdens poliklinische revalidatie na een CVA te onderzoeken. In **Hoofdstuk 4** wordt het studie protocol van de pragmatische RCT beschreven. Het onderzoek beoogt primair te onderzoeken of PST een effectieve groepsinterventie is voor het verbeteren van coping strategie en HR-QoL bij patiënten met een CVA. Secundair wordt gekeken naar het effect van PST op depressie, sociale participatie en gezondheidszorg consumptie, en naar de kosten-effectiviteit van de interventie. De methoden en opzet van de studie worden in detail beschreven, evenals de rationale en de inhoud van de interventie. De interventiegroep krijgt PST aanvullend op het standaard poliklinische revalidatieprogramma, de controlegroep krijgt alleen poliklinische revalidatie. De PST interventie bestaat uit acht groepsessies van 1,5 uur per week, met huiswerk oefeningen na elke sessie. Aan de groepsbijeenkomsten, gegeven door een getrainde neuropsycholoog, nemen 3-6 patiënten deel. Het probleemoplossend proces is gestructureerd in vier stappen: [1] definiëren van het probleem en doel; [2] genereren van meerdere oplossingen; [3] selecteren van een oplossing; en [4] uitvoeren en evalueren. Metingen, bestaand uit vragenlijsten en neuropsychologische tests, worden uitgevoerd voorafgaand aan, direct na de interventie, en zes en twaalf maanden later.

De resultaten van de RCT worden beschreven in **Hoofdstuk 5**. Coping strategie werd gemeten met de CISS, probleemoplossende vaardigheden met de SPSI-R:SF, depressie met de CES-D, en HR-QoL met de EQ-5D en de SS-QoL-12. CVA patiënten werden benaderd op poliklinische behandelafdelingen van Rijndam Revalidatiecentrum in Nederland en het Universitair Ziekenhuis Gent in België. In totaal werden 166 patiënten geïncludeerd in de studie. De resultaten laten zien dat de PST groep zes maanden na de interventie een significante verbetering toonde in vergelijking met de controlegroep in taakgerichte coping, maar niet in CVA-specifieke psychosociale HR-QoL. Daarnaast verbeterde vermijdende coping en de utiliteitscore voor generieke HR-QoL na zes maanden meer in de PST groep dan in de controlegroep. De resultaten suggereren dat PST een waardevolle interventie is voor CVA patiënten, die van aanvullende waarde kan zijn op de standaard poliklinische

revalidatie. PST lijkt taakgerichte coping te verbeteren en er zijn aanwijzingen dat PST het herstel van generieke HR-QoL en vermijdende coping kan verbeteren.

De derde doelstelling van dit proefschrift wordt beschreven in **Hoofdstuk 6**. Omdat wij geïnteresseerd waren in het verbeteren van HR-QoL, de ultieme uitkomstmaat op het gebied van revalidatie, vroegen we ons af of andere therapieën deze uitkomstmaat konden verbeteren. We voerden een systematische literatuurstudie en een meta-analyse uit om bewijsmateriaal uit de literatuur over de effectiviteit van revalidatie interventies na CVA samen te voegen en om te evalueren welke type interventie het meest effectief is. Een variëteit aan revalidatie interventies, bestudeerd middels RCT's of pre-post studies, werden geïnccludeerd. Primaire uitkomstmaten waren de 'Mental Component Score' (MCS) en 'Physical Component Score' (PCS) van de Short Form-36. Het literatuuronderzoek resulteerde in 581 artikelen. Uiteindelijk werden 32 artikelen opgenomen in de meta-analyse. In de pre-post designs werden 1728 patiënten geïnccludeerd, in de RCT's 1259. Zowel MCS als PCS verbeterden significant gedurende de interventieperiode. In de RCT studies verbeterde MCS significant in vergelijking tot de controle conditie, maar PCS niet. Er werden weinig verschillen gevonden in de effecten van de verschillende soorten interventies. De resultaten suggereren dat revalidatie interventies gericht op patiënten met een CVA effectief zijn in het verbeteren van HR-QoL op de korte termijn, het meest opvallend in de MCS. Er is weinig bewijs om te onderscheiden welke type interventie het meest effectief is.

In **Hoofdstuk 7** worden de belangrijkste bevindingen van dit proefschrift besproken. De inhoud van de PST interventie is geëvalueerd door de patiënten die deelnamen aan de PST groep. De resultaten van deze evaluatie worden gepresenteerd en bediscussieerd. Tot slot worden methodologische overwegingen, implicaties voor de klinische praktijk en toekomstperspectieven besproken. We concluderen dat coping strategie en depressie onafhankelijk zijn gerelateerd aan HR-QoL bij patiënten in zowel de chronische als de revalidatie fase na een CVA. Bij patiënten in poliklinische revalidatiebehandeling na een CVA verbetert PST taakgerichte coping en herstel van HR-QoL. Daarnaast lijkt PST vermijdende coping te verbeteren. Deze interventie lijkt een veelbelovende aanvulling op de poliklinische revalidatie na een CVA. Revalidatie interventies kunnen HR-QoL verbeteren, wat ook moet worden nagestreefd in een revalidatie behandeling na CVA. Dit proefschrift laat zien dat dit kan worden bereikt met behulp van de relatieve goedkope interventie Problem Solving Therapy.

Dankwoord

En dan nu het meest gelezen deel van een proefschrift, het woord van dank. Ik ga de uitdaging aan om deze kort en krachtig te houden, maar toch niemand te vergeten. Ik wil iedereen bedanken die op enige wijze betrokken is geweest bij de totstandkoming van dit proefschrift, en heeft bijgedragen aan de benodigde problem solving hieromheen. Een aantal mensen wil ik in het bijzonder bedanken.

Prof.dr. Ribbers, beste Gerard, dank voor het vertrouwen dat je in mij hebt gesteld en de mogelijkheden die je mij hebt gegeven. Je kritische blikken en commentaren waren leerzaam en waardevol. Prof.dr. van Busschbach, beste Jan, dank voor de begeleiding en de geboden mogelijkheden vanuit de MPP. Je kritische vragen over het waarom brachten vaak andere invalshoeken om verder te komen. Dr. Heijenbrok-Kal, beste Majanka, dank voor het vele meedenken, je onvermoeibaar kritische aanvullingen en natuurlijk de vele kopjes koffie. Ik ben heel erg blij dat jij als copromotor bij dit project betrokken bent geweest. Dr. van 't Spijker, beste Adriaan, dank voor de inhoudelijk waardevolle aanvullingen die jij vanaf de zijlijn hebt gegeven.

Bijzondere dank aan alle patiënten die aan dit onderzoek hebben meegedaan. Dank aan alle artsen die hebben geholpen met het werven van patiënten, en psychologen die hebben meegedacht en bijgedragen aan het geven van de groepen. Speciale dank aan Engelen en collega's uit Gent voor de enorme inzet en de prettige samenwerking. Onderzoeksassistentes, dank voor jullie hulp bij het afnemen van alle metingen, invoeren van de data en andere ondersteunende werkzaamheden. Receptionistes, baliemedewerkers en planning, dank voor alle hulp met betrekking tot de logistiek van de groepen. Loes, dank voor de ondersteuning vanaf de achtergrond.

Collega's van de Maasdamgang, dank voor alle gezelligheid, interesse en het meeleven de afgelopen jaren. Collega's van de MPP, dank voor de leuke dinsdagen, deze waren een waardevolle toevoeging op mijn werkweken. Collega's van het Erasmus, dank voor de gezelligheid en het kunnen delen van ervaringen. Collega's van het NIHC consortium Cognitieve Revalidatie, dank voor de leuke samenwerking. Mijn huidige collega's in het YSL wil ik bedanken voor de belangstelling tijdens de afrondende fase van dit proefschrift.

Mijn beide paranimfen wil ik bedanken dat ze naast mij willen staan op deze bijzondere dag. Heel speciaal dat ik de afgelopen twee maanden eerst naast jullie beiden mocht staan bij jullie promoties. Wendy, heel bijzonder hoe onze trajecten bijna

gelijk op zijn gelopen vanaf ons collegaschap als onderzoeksassistent. Bedankt voor alle steun, begrip, gezelligheid en plezier de afgelopen jaren, zowel binnen het onderzoek als daarbuiten. Willemien, heel bijzonder dat jij bijna tegelijkertijd een vergelijkbaar traject hebt doorlopen, al moest jouw onderzoek natuurlijk nèt iets eerder zijn afgerond. Bedankt voor alle hulp van afstand, je nuchtere blikken en vrolijke inbreng.

Mijn vrienden en familie wil ik allemaal bedanken voor de interesse maar vooral voor de nodige ontspanning en gezelligheid die het mogelijk maakten om dit proefschrift te kunnen schrijven. In het bijzonder wil ik hierbij nog mijn ouders, zussen en broer noemen. Deze warme, gezellige en nuchtere basis heeft mij gestimuleerd om te kunnen doen waar ik gelukkig van word.

Tot slot een woord voor Tim, het was niet altijd makkelijk voor jou als ik weer iets voor 'dat proefschrift' moest doen, zeker niet toen we samen ons nieuwe huis betrokken. Dank voor je begrip en geduld, rust en relativering, bedankt voor precies alles.

About the Author

Marieke Visser was born in Alkmaar on the 19th of March 1986. She attended secondary school at the Trinitas College (VWO) in Heerhugowaard, where she graduated in 2004. The same year she started her study Psychology at Leiden University. In 2007 she obtained her Bachelor's degree. She continued with a Master of Science in Clinical Neuropsychology, followed by a Master of Science in Clinical Psychology. She obtained her Master degrees in 2010. In august 2010 Marieke started working on the research described in this thesis at the Department of Rehabilitation Medicine of the Erasmus MC, Rotterdam as part of the research line Rotterdam Neurorehabilitation Research (RoNeRes). During her research, she started a Master of Science in Clinical Epidemiology at the Netherlands Institute of Health Sciences (NIHES). In 2013, she obtained her Master's degree in health sciences. Subsequently, she was active as a psychologist at two different outpatient departments of Rijndam Rehabilitation Center, diagnosing and treating patients with acquired brain injury and chronic pain. Currently, she continues her clinical work at the outpatient department of Rijndam Rehabilitation Center.

List of Publications

Visser MM, Heijenbrok-Kal MH, van 't Spijker A, Lannoo E, Busschbach JJV, Ribbers GM. Problem Solving Therapy during outpatient rehabilitation improves coping and HRQoL: randomized controlled trial. *Stroke*. 2016;47(1):135-42.

Visser MM, Heijenbrok-Kal MH, van 't Spijker A, Oostra KM, Busschbach JJV, Ribbers GM. Coping, problem solving, depression, and health-related quality of life in patients receiving outpatient stroke rehabilitation. *Archives of Physical Medicine and Rehabilitation*. 2015;96:1492-1498.

Visser MM, Aben L, Heijenbrok-Kal MH, Busschbach JJV, Ribbers GM. The relative effect of coping strategy and depression on health-related quality of life in patients in the chronic phase after stroke. *Journal of Rehabilitation Medicine*. 2014;46(6):514-519.

Visser MM, Heijenbrok-Kal MH, van 't Spijker A, Ribbers GM, Busschbach JJV. The effectiveness of problem solving therapy for stroke patients: study protocol for a pragmatic randomized controlled trial. *BMC Neurology*. 2013;13:67.

Aben L, Ponds RWHM, Heijenbrok-Kal MH, **Visser MM**, Busschbach JJV, Ribbers GM. Memory complaints in chronic stroke patients are predicted by memory self-efficacy rather than memory capacity. *Cerebrovascular Diseases*. 2011;31:566-572.

PhD Portfolio

Summary of PhD training and teaching

Name PhD student:	Marieke M. Visser	PhD period:	2010-2015
Erasmus MC Department:	Rehabilitation Medicine	Promotors:	Prof.dr. G.M. Ribbers
Research School:	Health Sciences		Prof.dr. J.J. van Busschbach
		Supervisor:	Dr. M.H. Heijnenbrok-Kal

1. PhD training

	Year	Workload (Hours/ECTS)
General courses		
• BROK course (Basiscursus Regelgeving Klinisch Onderzoek)	2011	30 hours
• CPO course	2011	7 hours
• Endnote course	2011	2 hours
• Cursus literatuur zoeken vervolg	2011	2 hours
• Writing a Scientific Article (Taalcentrum VU)	2012	64 hours
• Integrity in Scientific Research	2013	2 ECTS
• What's your story? - Storytelling training	2014	16 hours
• BROK course update	2015	3 hours
Research master NIHES: MSc in Health Science, specialisation 'Clinical Epidemiology'		
• 'Principles of Research in Medicine'	2011	0.7 ECTS
• 'Clinical Decision Analysis'	2011	0.7 ECTS
• 'Methods of Public Health Research'	2011	0.7 ECTS
• 'Markers and Prognostic Research'	2011	0.7 ECTS
• 'The Practice of Epidemiologic Analysis'	2011	0.7 ECTS
• 'Pharmaco-epidemiology'	2011	0.7 ECTS
• 'Study Design'	2011	4.3 ECTS
• 'Biostatistical Methods I: Basic Principles'	2011	5.7 ECTS
• 'Methodological Topics in Epidemiological Research'	2011	1.4 ECTS
• 'Biostatistical Methods II: Popular Regression Models'	2011	4.3 ECTS
• 'Courses for the Quantitative Researcher'	2012	1.4 ECTS
• 'Repeated Measurements in Clinical Studies'	2012	1.4 ECTS
• 'Preventing Failed Psychological Intervention Research'	2012	1.4 ECTS
• 'Topics in Meta-analysis'	2012	0.7 ECTS
• 'Logistic Regression'	2012	1.4 ECTS
• 'Clinical Epidemiology'	2012	5.7 ECTS
• 'Advanced Topics in Decision Making in Medicine'	2013	1.9 ECTS
• 'Quality of Life Measurement'	2013	0.9 ECTS
• 'Missing Values in Clinical Research'	2013	0.7 ECTS
• Research paper and presentation	2013	2.5 ECTS

Seminars and workshops

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|--|------|----------|
| • Emotions in Check and Problem Solved! Metacognitive Interventions for Individuals with Brain Injury: A Training Workshop, ACRM Vancouver | 2012 | 3 hours |
| • Introduction to Individual Growth Curve Analysis, ACRM Vancouver | 2012 | 3 hours |
| • Brain Injury Coping Skills (BICS) Workshop: An Intervention for Survivors of Brain Injury and Caregivers, ACRM Vancouver | 2013 | 3 hours |
| • Cognitive assessment at the stroke unit: from bedside testing to full neuropsychological assessment, INS Amsterdam | 2013 | 2 hours |
| • Attentional Disorders and Their Rehabilitation, INS Amsterdam | 2013 | 2 hours |
| • Cognitive Rehabilitation Training, ACRM Toronto | 2014 | 16 hours |

Oral presentations

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|--|------|----------|
| • 'Effectiveness of Problem Solving Therapy in stroke patients - Study design', neuroreferaat Rijndam Rehabilitation Center, Rotterdam | 2010 | 15 hours |
| • 'Effectiviteit Problem Solving Therapy for stroke patients', regional meeting for rehabilitation physicians, Rotterdam | 2011 | 15 hours |
| • 'Problem Solving Therapy in stroke patients', NIHC Pillar meeting Healthy Brain, Utrecht | 2012 | 8 hours |
| • 'Coping style and depression independently predict quality of life in chronic stroke patients', 9th World Congress on Brain Injury, Edinburgh, Scotland | 2012 | 20 hours |
| • 'Problem Solving Therapy in sub-acute stroke rehabilitation: a RCT', American Congress of Rehabilitation Medicine, Vancouver, Canada | 2012 | 20 hours |
| • Workshop 'Problem Solving Therapy', Brain Awareness Week 2013, Den Haag | 2013 | 10 hours |
| • 'The relative effect of coping style and depression on quality of life in chronic stroke patients', 10th Conference of the Neuropsychological Rehabilitation Special Interest Group of the WFNR, Maastricht, the Netherlands | 2013 | 10 hours |
| • 'Relationships between problem solving skills, depression and health-related quality of life during outpatient rehabilitation for stroke', 11th Conference of the Neuropsychological Rehabilitation Special Interest Group of the WFNR, Limassol, Cyprus | 2014 | 12 hours |
| • 'PST-training na een CVA: (hoe) werkt het?', Hersenletselcongres, Ede | 2014 | 20 hours |
| • 'Problem Solving Therapy During Outpatient Rehabilitation for Stroke: Short-term Results of a Randomized Controlled Trial', DCRM Annual Congress 2014, Rotterdam | 2014 | 12 hours |
| • 'PST-training na een CVA: (hoe) werkt het?', najaarsconferentie NIP sectie Revalidatie | 2014 | 12 hours |
| • Workshop 'Problem Solving Therapy na CVA: hoe werkt het?', Landelijk Symposium Cognitieve Revalidatie, Amersfoort (3x) | 2015 | 12 hours |
| • 'Problem Solving Therapy na een CVA: (hoe) werkt het?', Studiedag samenwerkingsverband NAH, Gent, Belgium | 2015 | 8 hours |
| • 'Problem Solving Therapy during outpatient rehabilitation for stroke', Congress on NeuroRehabilitation and Neural Repair, Maastricht | 2015 | 12 hours |

- 'Problem Solving Therapy na CVA: (hoe) werkt het?', Wetenschapscafé Blixembosch, Eindhoven 2015 8 hours
- Problem Solving Therapy during Outpatient Stroke Rehabilitation Improves Coping and HR-QoL: a Randomized Controlled Trial, 11th World Congress on Brain Injury, Den Haag, Nederland 2016 20 hours

Poster presentations

- 'Effectiveness of Problem Solving Therapy in stroke patients', HCMI congress, Utrecht 2011 8 hours
- 'The effectiveness of Problem Solving Therapy for stroke patients: study protocol for a pragmatic randomized controlled trial', VRA Annual Congress 2013, Noordwijkerhout, the Netherlands 2013 8 hours
- 'Problem Solving Therapy During Outpatient Rehabilitation for Stroke: Short-term Results of a Randomized Controlled Trial', HCMI Health Pillar Meeting 2014 16 hours
- 'Problem Solving Therapy During Outpatient Rehabilitation for Stroke: Short-term Results of a Randomized Controlled Trial', ACRM, Toronto 2014 16 hours
- 'Problem Solving Therapy voor CVA-patiënten: korte termijn effecten van een RCT', Breinproductendag NIHC, Utrecht 2014 8 hours
- 'Problem Solving Therapy during outpatient rehabilitation for stroke: long-term results of a randomized controlled trial', Dutch Congress of Rehabilitation Medicine, Rotterdam 2015 8 hours

(Inter)national conferences

- Nederlandse Vereniging voor Neuropsychologie (NVN), Antwerpen, Belgium 2012 8 hours
- 9th World Congress on Brain Injury (IBIA), Edinburgh, Scotland 2012 24 hours
- American Congress of Rehabilitation Medicine, Vancouver, Canada 2012 36 hours
- 10th conference of the Neuropsychological Rehabilitation Special Interest Group of the World Federation for NeuroRehabilitation (WFNR), Maastricht, the Netherlands 2013 16 hours
- International Neuropsychological Society, mid-year meeting, Amsterdam, the Netherlands 2013 28 hours
- VRA Annual Congress 2013, Noordwijkerhout, the Netherlands 2013 16 hours
- 11th conference of the Neuropsychological Rehabilitation Special Interest Group of the World Federation for NeuroRehabilitation (WFNR), Limassol, Cyprus 2014 16 hours
- American Congress of Rehabilitation Medicine, Toronto, Canada 2014 36 hours
- Hersenletselcongres, Ede, the Netherlands 2014 8 hours
- Dutch Congress of Rehabilitation Medicine, Rotterdam, the Netherlands 2014 16 hours
- NIP Sectie Revalidatie, Eindhoven, the Netherlands 2014 8 hours
- Congress on NeuroRehabilitation and Neural Repair, Maastricht, the Netherlands 2015 16 hours
- 11th World Congress on Brain Injury, Den Haag, Nederland 2016 8 hours

Other

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|---|-----------|-----------|
| • Participating in research meetings, dept. of Rehabilitation Medicine, Rotterdam | 2010-2015 | 180 hours |
| • Participating in research meetings, dept. of Medical Psychology and Psychotherapy, Rotterdam | 2010-2015 | 90 hours |
| • Organizing and participating in RoNeRes journal club, dept. of Rotterdam Neurorehabilitation Research | 2013-2015 | 17 hours |
| • Review scientific articles for international journals | 2014 | 40 hours |
| • Organizing HCMI Health Pillar Meeting | 2014 | 40 hours |
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2. Teaching**Other**

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| • Supervising literature review medical students | 2011 | 16 hours |
| • Supervising literature review medical students | 2012 | 16 hours |
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