

ORIGINAL REPORT

A PROSPECTIVE STUDY ON COPING STRATEGIES AND QUALITY OF LIFE IN PATIENTS AFTER STROKE, ASSESSING PROGNOSTIC RELATIONSHIPS AND ESTIMATES OF COST-EFFECTIVENESS

Anne-Sophie E. Darlington, PhD¹, Diederik W. J. Dippel, MD, PhD², Gerard M. Ribbers, MD, PhD^{3,4}, Romke van Balen, MD, PhD⁵, Jan Passchier, PhD¹ and Jan J. V. Busschbach, PhD^{1,6}

From the ¹Department of Medical Psychology and Psychotherapy and ²Department of Neurology, Erasmus MC, ³Rijnndam Rehabilitation Centre and ⁴Department of Rehabilitation Medicine, Erasmus MC, ⁵Antonius Binnenweg Nursing Home and Geriatric Centre, Rotterdam and ⁶Viersprong Institute for Studies on Personality Disorders, Halsteren, The Netherlands

Objective: To examine the prognostic value of coping strategies of patients after stroke at time of discharge on quality of life approximately one year later. In addition, we estimated the maximum cost of improving quality of life by enhancing coping strategies using strict assumptions.

Methods: Eighty patients with a stroke completed several questionnaires, at discharge to home and 9–12 months later (follow-up). Questionnaires measured quality of life, coping strategies Tenacious Goal Pursuit and Flexible Goal Adjustment. First, a regression analysis was carried out predicting quality of life at follow-up from coping strategies at discharge. Secondly, a maximum in terms of acceptable cost was calculated for several possible effect sizes.

Results: Both coping strategies at discharge were positively associated with quality of life at follow-up. With regards to cost-effectiveness, a medium effect size would result in an increase in quality of life of approximately 10%. The maximum acceptable cost of an intervention for a single patient is therefore set at €2500, assuming a benefit of one year and a cost per quality adjusted life year of €25,000.

Conclusion: Coping strategies at discharge are predictive of quality of life one year later. The costs of improving quality of life are thought to be within the limits that determine a cost-effective intervention.

Key words: cost-effectiveness, stroke, quality of life, coping.

J Rehabil Med 2009; 41: 237–241

Correspondence address: Anne-Sophie E. Darlington, Erasmus University Medical Center, Department of Medical Psychology and Psychotherapy, Dr. Molewaterplein 50 NL-3015 GE Rotterdam, The Netherlands. E-mail: a.darlington@erasmusmc.nl

Submitted March 10, 2008; accepted October 8, 2008

INTRODUCTION

Quality of life (QoL) is known to be impaired in patients after stroke, and in the immediate period after a stroke this is largely due to reduced physical functioning (1–4). However, notwithstanding a similar degree of impairment, patients after stroke differ in the relative reduction they experience in QoL. Differences in coping styles, which refers to a person's cogni-

tive and emotional abilities to handle events that are perceived as stressful, are believed to play a part in this (5–9). Indeed, patients were interviewed 3 years after their stroke and were asked about their preferred coping strategies in dealing with the stroke. Results showed that patients with a preference for active coping strategies, rather than passive, avoidant or emotional coping, were found to show better improvement on activities of daily living (8). In addition, a small study investigated coping strategies as defined by Brandstädter & Renner (9), who classify coping strategies into Tenacious Goal Pursuit (TGP), whereby a person actively adjusts circumstances in order to strive to maintain life as it was before, and Flexible Goal Adjustment (FGA), whereby a person attempts to accept the consequences of the stroke by adjusting personal preferences and goals (10). These 2 coping strategies were investigated in a group of 8 relatively younger patients after stroke and evidence was found for a positive relationship between coping strategy FGA whereby the patient attempts to accept changes, and QoL (10). A recent cross-sectional study found that, in fact, both these coping strategies were positively related to QoL, but only approximately 5 months after discharge (6). The results of that study show that finding a balance between accepting changes and striving to maintain life as it was before results in the best outcome in terms of QoL. Authors of a recent review reiterate this point by highlighting the importance of coping strategies especially when it comes to the rehabilitation process (11). Therefore, future interventions aimed at improving QoL would do well to focus on coping strategies (12). This is especially important in light of the reported lack of theoretical basis in complex interventions in patients after stroke to date (13).

Another question relevant to future interventions aimed at improving QoL through coping is whether an intervention could in fact be cost-effective. There is currently a lack of data regarding interventions for patients after stroke that are aimed at improving or addressing coping strategies. However, a recent intervention study, which was aimed at reducing levels of depression in post-stroke patients, investigated the effectiveness of Problem-Solving Therapy (14). This intervention methodology is geared towards addressing cognitive appraisal of problems and the way the problems are solved. This is, in essence, a means of improving the way in which patients cope

with the changes in their life (15). This is an example of an intervention methodology that has previously been applied to patients with different chronic conditions, such as chronic pain and cancer, with the aim of improving functioning (16, 17). Thus, the question is whether an intervention for patients after stroke can be cost-effective. While cost-effectiveness analyses have been carried out on interventions aimed at caregivers, such information is not available for interventions aimed at improving QoL through coping strategies (18).

While a relationship between coping and QoL in patients after stroke has been found (6–8, 10), these studies have been cross-sectional in nature. It is not yet clear to what extent coping strategies at time of discharge to home are indicative of QoL in the long term. In the current study we were especially interested in coping strategies of patients who are discharged to home, since it is likely that the reality of a patient's current status is most apparent in the home environment, therein forcing the patient to make use of effective coping strategies.

Thus, the first aim of the study was to investigate the longitudinal relationship between coping strategies at discharge and QoL approximately 9–12 months after discharge. The second aim of the current study was to estimate the maximum acceptable cost price, based on the longitudinal data using quality adjusted life year (QALYs), of improving QoL by enhancing a patient's coping strategies after stroke.

METHODS

Patients

The study concerned patients with a first-ever stroke, defined as cerebral infarction, infarction from cerebral venous sinus thrombosis, or intracerebral haematoma. Patients were included in the study at the time-point of discharge from hospital, rehabilitation centre, or nursing home to their homes, but not longer than 6 months after onset of stroke. The sample consisted of patients who were discharged to go home, since coping with the reality of the impact on daily living was expected to start upon the return to the home environment. Patients were excluded according to the following criteria: (i) modified Rankin Scale score (mRS) > 3 (19, 20); (ii) severe language impairment; (iii) insufficient grasp of the Dutch language; (iv) severe co-morbidity prohibiting participation in the study, or thought to influence coping and QoL over and above the experienced stroke; and (v) no written informed consent given. With regard to language or cognitive impairment the physician's clinical assessment was the basis for excluding patients. Patients were recruited, consecutively, by the physician in charge of their treatment, whilst admitted to the Erasmus MC, the Rijndam Rehabilitation Centre or one of 3 dedicated nursing homes in Rotterdam from February 2003 to February 2004. All patients who were discharged to go home during this period were asked to participate. A negligible number of patients ($n=2$) declined to participate. The centres in this study participate in one regional stroke service; stroke treatment and stroke care were delivered according to national guidelines (21).

Study design

The study consisted of assessments at 4 different time-points no more than one week before discharge, 2 months after discharge, 5 months after discharge, and 9–12 months after discharge, although data from only 2 time-points will be discussed here (6): at discharge no more than one week before discharge, and at follow-up, 9–12 months after discharge. At discharge patients completed the questionnaires whilst still admitted to the hospital, rehabilitation centre of nursing home, and were discharged no later than one week after being recruited for the study. Patients were

asked to complete questionnaires at each time-point measuring QoL (EQ-5D) (22), and coping strategies (assimilative-accommodative coping scale) (19). General functioning and disability was assessed by means of the mRS (19, 20). Approval for the study was obtained from the institutional medical ethics committee and review board. Written informed consent was obtained from all patients before the start of data collection.

Measures

QoL, measured at follow-up. The EQ-5D is a self-report QoL questionnaire consisting of 5 items pertaining to mobility, self-care, usual activities, pain/discomfort, anxiety/depression (22). For each domain patients indicate whether they experience either no problems, some/moderate problems or extreme problems. The items can be summarized into one weighted overall score, which runs from 0 for the least desirable health state (death) to 1.00 for full health. The EQ-5D has been shown to be a valid measure to use in research concerning patients after stroke (23). The EQ-5D is also a utility measure, in that utility weights can be applied to the different health states of the EQ-5D, which can subsequently be used to calculate QALYs.

Coping, measured at discharge. The Assimilative-Accommodative Coping Scale is a self-report questionnaire which consists of 2 subscales; Tenacious Goal Pursuit (TGP) refers to the coping strategy that is aimed at actively adjusting circumstances to personal preferences, and thus striving to maintain life as it was before the stroke and Flexible Goal Adjustment (FGA) refers to the coping strategy whereby the patient attempts to accept the consequences of the stroke by adjusting personal preferences and goals. Each subscale contains 15 items and questions are answered on a 5-point Likert scale, ranging from "strongly agree" to "strongly disagree" (0–4) (9). A mean score of each subscale is calculated, ranging from 0 to 4, and higher scores indicate that a patient tends to use that coping strategy more. An example item for TGP is "When faced with difficulties I usually double my efforts" and an example item for FGA is "I adapt quite easily to changes in plans or circumstances". Internal consistency and validity of the scale range is reported to be good. The Dutch translation of the questionnaire was used and the scale was made situation-specific to increase its sensitivity (24).

General functioning, measured at discharge. General functioning and disability was measured by the mRS (19, 20).

Data analysis

Regression analysis of coping and QoL. Baseline characteristics are presented in terms of percentages and means (standard deviation (SD)). Univariable relationships between the baseline characteristics and QoL at follow-up are calculated by means of Pearson correlations and analysis of variance (ANOVAs). The predictive value of coping strategies at discharge on QoL at follow-up was examined by means of a multiple linear regression analysis. QoL at follow-up measured by the EQ-5D, was entered as the dependent variable and the coping variables TGP and FGA at discharge were entered as independent variables. Age, sex and mRS at discharge, (converted into 2 dummy variables: mRS 2, mRS 3) were included to control for their influence.

Cost-effectiveness methodology. To outline the cost-effectiveness of enhancing coping strategies in order to improve QoL was translated in terms of Cohen's d (25). Cohen's d is a universal way of interpreting effect sizes that is commonly used in social science, and is defined as the difference between the means divided by the SD: $d = (M1 - M2) / SD_{\text{pooled}}$. Cohen (25) defined effect sizes as "small, $d=0.2$; medium $=0.5$ and large $=0.8$ " (25). For each different effect size the increase in QoL was determined, given an improvement in both coping strategies (TGP and FGA). These calculations were carried out using the unstandardized Bs generated from the regression analysis. This calculation generated the actual increase in QoL achieved by improving both coping strategies. Subsequently, QALYs are used to determine the cost of the possible intervention and can be calculated from QoL measures. In the current study increases in QoL are measured

by the EQ-5D index. In a QALY analysis, time is multiplied by an index factor for the QoL. For instance, 3 years with a QoL of 0.5, would be 1.5 QALYs. The crucial factor in cost-effectiveness evaluation is the size of the cost-effectiveness ratio; here the amount of money society is willing to spend to increase the number of QALYs. In the analyses in this study the maximum cost per QALY will initially be set at €25,000 (26, 27). Data will also be presented for analyses applying €50,000 and €80,000 per QALY. In the current study another assumption was made with regard to the analyses. The intended effect of an intervention will last for one year, and initial analyses will be conducted on the basis of this assumption.

RESULTS

Patients

The cohort consisted of 80 patients (Table I). The mean age was 60.9 years (SD 16.9), and 51% was female ($n=41$). At discharge the majority of patients had mRS 2 (56%) or mRS 3 (28%). At follow-up questionnaire data for 62 patients was collected. Data was not available for a total of 18 patients; 6 patients did not want to participate at some time during follow-up, 2 patients moved, 2 were admitted to hospital, one died, and 7 did not return their questionnaire. Comparative analyses showed that those patients whose data was missing at follow-up differed from the remainder of the sample as measured at discharge only on FGA (2.36 vs 2.75, respectively, $p<0.05$). The measurement at follow-up was conducted on average 10.9 (SD 1.19) months after discharge. Mean QoL at follow-up was 0.72 (SD 0.224). Demographic and medical data, and mean levels of coping and

QoL are shown in Table I. Interestingly, FGA and TGP were not correlated ($r=-0.10$, $p=0.39$), confirming the questionnaire structure containing 2 separate subscales. More detailed information has been presented elsewhere (6). Univariable analyses of the baseline characteristics and QoL at follow-up are presented in Table II. No significant relationships were found.

Determining QoL from coping strategies

Regression analysis showed that FGA at discharge significantly predicted QoL at follow-up (beta=0.126, 95% confidence interval (CI): 0.033; 0.219, $p<0.01$), with higher levels of FGA corresponding to higher levels of QoL. TGP was also positively associated with QoL at follow-up, although this relationship did not reach statistical significance (beta=0.074, 95% CI: -0.010; 0.158, $p=0.083$). General functioning at discharge, as measured by the mRS, sex and age, did not predict QoL at follow-up (Table III). When missing QoL data in the 18 patients with incomplete follow-up were substituted with data from observations at approximately 2 or 5 months (last observation carried forward), the results of the regression analysis were not affected.

Cost-effectiveness of improving coping strategies

The results indicate that, for a small effect size (Cohen's d 0.2), QoL is likely to improve approximately 0.04 on a scale from 0.00 to 1.00, according to the formula: $\text{Increase QoL} = (d \times \text{unstandardized } B \text{ TGP}) + (d \times \text{unstandardized } B \text{ FGA})$, where d is the effect size and using the unstandardized betas, corrected for sex, age, mRS2 and mRS3, from the regression analysis presented in Table II: increase in QoL = $(0.2 \times 0.126) + (0.2 \times 0.074)$. With a medium effect size (Cohen's d 0.5) QoL is increased by approximately 0.10, or expressed in terms of percentages increased by 10%. A large effect size increases QoL by 0.16.

Assuming a maximum of €25,000 per QALY and an enduring effect spanning a year, the maximum costs of improving QoL

Table I. Baseline characteristics of patients ($n=80$)

Characteristics	At discharge
Age, years, mean (SD)	60.9 (16.9)
Women, n (%)	41 (51)
Education level, n (%)*	
None	1 (1)
Primary	26 (33)
Secondary	31 (39)
Higher	21 (26)
Diagnosis, n (%)	
Ischaemic stroke	63 (79)
Intracerebral hematoma	16 (20)
Venous sinus thrombosis	1 (1)
Time since admission, weeks, median (range)	5.4 (0.1–37.6)
Hospital	0.8 (0.1–4.0)
Rehabilitation	9.8 (4.0–25.1)
Nursing home	11.1 (5.3–37.6)
Discharge from, n (%)	
Hospital	39 (49)
Rehabilitation centre	22 (27)
Nursing home	19 (24)
mRS 0, n (%)	5 (6)
mRS 1, n (%)	8 (10)
mRS 2, n (%)	45 (56)
mRS 3, n (%)	22 (28)
EQ-5D score at follow-up, mean (SD)	0.72 (.22)
Coping TGP at discharge, mean (SD)	2.21 (.73)
Coping FGA at discharge, mean (SD)	2.66 (.64)

*Missing information for one patient.

SD: standard deviation; mRS: Modified Rankin Scale; TGP: Tenacious Goal Pursuit, score range 0–4; FGA: Flexible Goal Adjustment, score range 0–4.

Table II. Univariable analyses of baseline characteristics and quality of life (QoL) at follow-up

Variable	Mean QoL score at follow-up	Statistics and p -value
Age		$r=-0.22$, $p=0.088$
Sex		
Men	0.70	
Women	0.74	$t=-0.68$, $p=0.499$
Education level		
Primary	0.69	
Secondary	0.69	
Higher	0.82	$F=2.07$, $p=0.13$
Time since admission		$r=-0.19$, $p=0.13$
Discharge from		
Nursing home	0.77	
Rehabilitation centre	0.69	
Hospital	0.64	$F=2.05$, $p=0.14$
mRS		
mRS 0 or 1	0.80	
mRS 2	0.72	
mRS 3	0.69	$F=1.00$, $p=0.37$

mRS: Modified Rankin Scale.

Table III. Unstandardized betas generated from the regression analysis: Outcome variable quality of life (QoL) (EQ-5D) at follow-up, and coping variables Tenacious Goal Pursuit (TGP) and Flexible Goal Adjustment (FGA) at discharge as determinants

Independent variables	Univariable			Multivariable model 1*			Multivariable model 2†		
	Beta	95% CI	p	Beta	95% CI	p	Beta	95% CI	p
TGP	0.070	−0.004 to 0.144	0.065	0.068	−0.012 to 0.150	0.093	0.074	−0.010 to 0.158	0.083
FGA	0.116	0.026 to 0.207	0.013	0.124	0.032 to 0.215	0.009	0.126	0.033 to 0.219	0.009

*Unstandardized betas adjusted for age and sex, total $n=62$.

†Unstandardized betas adjusted for age, sex and mRS2 and mRS3.

95% CI: 95% confidence interval; mRS: Modified Rankin Scale.

through coping strategies with median effect is €2500 in order to still be considered cost-effective. If the effect size is assumed to be larger, or if we assume higher acceptable costs per QALY, improving QoL may be more costly (Fig. 1). A maximum cost price of €2500 would be a realistic benchmark for a possible limited psychosocial intervention, especially group interventions.

DISCUSSION

This study shows that variance in coping just after stroke is related to long-term QoL. Higher levels of the coping strategy FGA, which represents the tendency to adjust personal preferences when a situation has changed, at discharge corresponded to higher levels of QoL approximately 9–12 months later. A similar relationship was found for the coping strategy TGP, which refers to the tendency to adjust aspects of one's situation, although this variable did not reach statistical significance. The importance of the relationship between FGA and QoL is supported by previous findings. A study using the same definition of coping strategies found a positive relationship between both FGA and QoL 5 months after discharge (6). In a smaller study on relatively young patients the coping strategy FGA was found to be related to QoL between 1 and 3 years after the stroke (10). The positive relationship between coping strategy TGP and QoL has been reported, and

is also in line with the finding of an association of active coping and QoL in patients after stroke (6, 8). However, the relationship between TGP and QoL in the current study did not reach statistical significance. This may be due to the relatively small sample size. The direction of the relationships support the notion that both coping strategies, as measured in the current study, are in fact important in determining QoL, and therefore both were included in the analyses concerning cost-effectiveness.

The analyses of cost-effectiveness showed that improving QoL through amending coping strategies, with a medium effect size and the maximum cost set at €2500, has the potential to be cost-effective. With the increasing numbers of patients with a stroke and therefore the increasing numbers of patients likely to be left with impaired functioning, regardless of severity, an improvement in QoL realized through enhancing coping strategies is something that should be seriously considered. The importance of focusing on coping strategies has recently been highlighted in a review on coping in patients after stroke (11). It is also likely that besides a direct effect of an intervention in terms of an improvement in QoL, an indirect knock-on effect is attainable when it comes to, for instance, healthcare utilization (18). If we assume that the effective intervention is accompanied by savings elsewhere, such savings could be subtracted from the cost of the intervention. In that case the maximum cost of an intervention could be increased.

The estimates made in this study rest on a number of assumptions. First of all, the assumption that a future psychosocial intervention would be able to improve QoL by enhancing coping strategies. There are several examples in the behavioural medicine literature that have shown to be effective in achieving this in different patient populations (16, 17). Specifically, very recently an intervention, referred to as Problem-Solving Therapy, has been used to reduce levels of depression in stroke patients. This intervention strategy aims to alter the way in which patients assess and solve their problems, thereby improving the way they cope with the changes that have occurred in their life as a result of the stroke (14). Secondly, the assumption was made that a national threshold exists for cost per QALYs. The level, and even the existence, of such thresholds is not without dispute (26, 27). The third assumption is that the effect of improving coping strategies on QoL would last for one year. Obviously, when we assume that the effects hold longer, the maximum acceptable costs for an effective treatment may rise. Considering the high incidence of stroke, budgetary constraints may play a role in setting a maximum cost for the intervention. This, however, is outside the scope of this study.

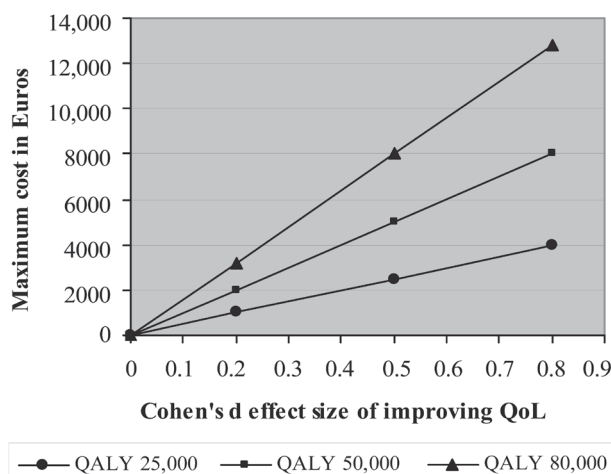


Fig. 1. Maximum acceptable cost of an intervention to improve quality of life (QoL) by enhancing coping strategies of patients with a recent stroke (y axis), expressed in Euros, as a function of a treatment effect, expressed as Cohen's d, for several levels of the cost-effectiveness ratio, expressed in cost (€) per quality adjusted life year (QALY).

This study concerned patients who could be discharged to home, in the majority of cases after clinical rehabilitation. This implies that its results and conclusions are limited to those with relatively mild strokes who could, to some degree, function independently. Another limitation is to do with sample size, which was relatively small, and there was substantial drop-out over the course of the study. A final limitation concerns the potential bias that may have occurred regarding the results of the coping strategy FGA. The sample of patients that was used in the final analysis differed from the group of patients available at baseline, on that specific coping strategy. The patients included in the final analyses had significantly higher levels of FGA than patients who dropped out during the course of the study. Therefore the results should be interpreted with this in mind, and more research is warranted, with a larger sample of patients after stroke, in order to replicate these findings. One of the strengths of this data-set, however, was its longitudinal nature, which enabled the assessments of the predictive value of coping strategies at discharge on QoL in the long term. In addition, QoL was measured by the EQ-5D, which is a utility measure that can be related to QALYs, thus allowing us to calculate cost-effectiveness parameters.

In conclusion, the results of this study have shown that initial coping strategies predict QoL during follow-up in stroke. In particular, FGA, which is a patient's tendency to be able to adjust goals, which aids in acceptance of changes, seems to matter. So far, the influence of coping on QoL has predominantly been studied cross-sectional designs (8, 10). The costs of improving QoL with an intervention of moderate effect size on coping strategies are probably within the limits that determine a cost-effective intervention. That means that it might be worthwhile to investigate further the possibility of such an intervention in order to maximize QoL in this patient group when options in terms of improvement of physical functioning have in essence been exhausted. Future research should see an investigation in which the effectiveness of an intervention is assessed in a randomized clinical trial. The trial should assess to what extent coping skills can be improved upon, thereby subsequently improving QoL, and to what extent this is in accordance with the currently presented results. In addition, the actual costs of such an intervention need to be investigated, as this is an increasingly important matter in healthcare economics.

ACKNOWLEDGEMENT

The study was supported by a grant from the Erasmus MC Revolving Fund. Grant number: 2002-1024.

REFERENCES

1. Sturm JW, Donnan GA, Dewey HM, Macdonell RA, Gilligan AK, Srikanth V, et al. Quality of life after stroke: the North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke* 2004; 35: 2340-2345.
2. Ebrahim S, Barer D, Nouri F. Use of the Nottingham Health Profile with patients after a stroke. *J Epidemiol Community Health* 1986; 40: 166-169.
3. Wyller TB, Holmen J, Laake P, Laake K. Correlates of subjective well-being in stroke patients. *Stroke* 1998; 29: 363-367.
4. King R. Quality of life after stroke. *Stroke* 1996; 27: 1467-1472.
5. Lazarus RS, Folkman S, editors. *Stress, appraisal, and coping*. New York: Springer; 1984.
6. Darlington ASE, Dippel DWJ, Ribbers GM, van Balen R, Passchier J, Busschbach JJV. Coping strategies as determinants of quality of life in stroke patients: a longitudinal study. *Cerebrovasc Dis* 2007; 23: 401-407.
7. Nydevik I, Hulter-Asberg K. Sickness impact after stroke. A 3-year follow-up. *Scand J Prim Health Care* 1992; 10: 284-289.
8. Emståhl S, Sommer M, Hagberg A. A 3-year follow-up of stroke patients: relationships between activities of daily living and personality characteristics. *Arch Gerontol Geriatr* 1996; 22: 233-244.
9. Brandstädter J, Renner G. Tenacious goal pursuit and flexible goal adjustment: explication and age-related analysis and assimilative and accommodative strategies of coping. *Psychol Aging* 1990; 5: 58-67.
10. Smout S, Koudstaal PJ, Ribbers GM, Janssen WGM, Passchier J. Struck by stroke: A pilot study exploring quality of life and coping patterns in younger patients and spouses. *Int J Rehabil* 2001; 24: 216-268.
11. Donnellan C, Hevey D, Hickey A, O'Neill D. Defining and quantifying coping strategies after stroke: a review. *J Neurol Neurosurg Psychiatry* 2006; 77: 1208-1218.
12. Dennis M, O'Rourke S, Slattery J, Staniforth T, Warlow C. Evaluation of a stroke family care worker: results of a randomised controlled trial. *BMJ* 1997; 314: 1071-1079.
13. Redfern J, McKevitt C, Wolfe C. Development of complex intervention in stroke care. A systematic review. *Stroke* 2006; 37: 2410-2419.
14. Robinson RG, Jorge RE, Moser DJ, Acion L, Solodkin A, Small SL, et al. Escitalopram and problem-solving therapy for prevention of poststroke depression: a randomised controlled trial. *JAMA* 2008; 299: 2391-2400.
15. Nezu AM, Nezu CM, Felgoise SH, McClure KS, Houts PS. Project Genesis: assessing the efficacy of problem-solving therapy for distressed adult cancer patients. *J Consult Clin Psychol* 2003; 71: 1036-1048.
16. Doorenbos A, Given B, Given C, Verbitsky N, Cimprich B, McCorkle R. Reducing symptom limitations: a cognitive behavioral intervention randomized trial. *Psychooncology* 2005; 14: 574-584.
17. Van den Hout JHC, Vlaeyen JWS, Heuts PHTG, Zijlema JH, Wijnjen JA. Secondary prevention of work-related disability in non-specific low back pain: does Problem-Solving Therapy help? A randomised clinical trial. *Clin J Pain* 2003; 19: 87-96.
18. Patel A, Knapp M, Evans A, Perez I, Kalra L. Training care givers of stroke patients: economic evaluation. *BMJ* 2004; 328: 1102.
19. de Haan R, Limburg M, Bossuyt P, van der Meulen J, Aaronson N. The clinical meaning of Rankin "handicap" grades after stroke. *Stroke* 1995; 26: 2027-2030.
20. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke* 1988; 19: 604-607.
21. Stroke guideline. Dutch Institute for Healthcare improvement (CBO) in collaboration with the Netherlands Heart Foundation. Alphen a/d Rijn: Van Zuiden Communications; 2000.
22. Dolan P. Modeling valuations for the EuroQol health states. *Medical Care* 1997; 35: 1095-1108.
23. Dorman PJ, Waddell F, Slattery J, Dennis M, Sandercock P. Is the EuroQol a valid measure of health-related quality of life after stroke? *Stroke* 1997; 28: 1876-1882.
24. Slangen-de Kort Y, editor. A tale of two adaptations: coping processes of older persons in the domain of independent living [PhD Thesis]. Eindhoven: Eindhoven University of Technology; 1999.
25. Cohen J, editor. *Statistical power analysis for the behavioral sciences* (2nd edn). Hillsdale, NJ: Lawrence Earlbaum Associates; 1988.
26. Devlin N, Parkin D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health Econ* 2004; 13: 437-452.
27. Pearson SD, Rawlins MD. Quality, innovation, and value for money: NICE and the British National Health Service. *JAMA* 2005; 294: 2618-2622.