Determinants of Health Status After Stroke: A Cohort Study with Repeated Measurements

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ORIGINAL RESEARCH

Determinants of Health Status After Stroke: A Cohort Study with Repeated Measurements

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Background: Knowledge about the long-term course of health following stroke is sparse and relies mainly on studies with short follow-up or few measurements per patient. We aimed to describe the course and analyze the determinants of the course of physical and mental health status after stroke with repeated measurements in a large population-based cohort of first time Danish stroke patients.

Methods: We followed 2,414 first time stroke patients admitted to any hospital in the Central Denmark Region, Denmark, between October 1, 2008 and January 1, 2012, with five questionnaires over a 2 years period. Self-rated health was assessed by the SF-12 instrument. Information on possible clinical and patient-related determinants of self-rated health was obtained from questionnaires and national registers. The scores were analyzed at five selected fixed time-points and as well as longitudinally with mixed models.

Results: The SF-12 mental component summary score (MCS) increased with 0.89 points/year (95% CI=0.6–1.2), while the increase in the physically component summary score (PCS) did not reach statistical significance (0.13/year; 95% CI=−0.2–0.5). The most pronounced changes were seen in the Vitality and Role Physical SF-12 subscales, which both increased by 2.1 points/year. No statistically significant changes over time were found in the Physical Functioning and Bodily Pain subscales. Variables associated with increasing self-rated mental health (MCS) were no comorbidity, older age, male gender, and mild stroke severity. Variables associated with increasing ratings of physical health (PCS) were mild stroke severity, no comorbidity, higher educational level, and younger age. The negative impact of age increased significantly with time during the follow-up period for physical as well as mental health, while the effects of the other variables were stable over time. The results were similar in the two analytical approaches.

Conclusion: In a large, geographically well-defined population of first time stroke patients, the majority of SF-12 sub-scales and the mental component score improved slightly over time. Small improvements in self-rated mental health may be observed during the first 2 years after the stroke. Stroke is a disease with long-term consequences on a wide range of health aspects. Level as well as course differ between sub-groups, and treatment of comorbidity may be an important target with respect to rehabilitation.

Keywords: cohort studies, patient-reported outcome, repeated measurements, self-rated health, stroke

Introduction

Stroke is a leading cause of mortality and disability. Improved management of stroke has led to increased survival rates resulting in more stroke survivors living with varying levels of disability.[1,2] Stroke is a condition that potentially affects the functional level as well as mental capacity and the ability to reintegrate in

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social life,[3,4] and stroke patients report their health as substantially lower than healthy referents.[5–7] Previous longitudinal studies on self-rated health after stroke have suggested stroke severity, co-morbidity, depression, fatigue, higher age, female gender, low educational level, and living alone as determinants of low self-rated health.[5,7–20] However, the results are partly conflicting. Most studies on stroke survivors have been conducted in the sub-acute phase with short follow-up time or in selected groups such as patients referred to rehabilitation. Furthermore, studies with longer follow-up most often rely on only one or few measurements or are limited by small sizes of cohorts.[3,5,7,9–18] As the number of survival years after stroke are increasing, the importance of knowledge of long-term prognosis of health also increases. We aimed to examine the course and the determinants of course of self-rated health with repeated measurements from 3–24 months after stroke in a large well defined cohort of first time stroke patients.

Patients and Methods
Study Population
We identified all patients with first-time stroke, who had been admitted to any hospital in the Central Denmark Region between October 1, 2008 and January 1, 2012. Central Denmark Region is one of five administrative units in Denmark with 1.2 million inhabitants.[21] During the study period, the region was served by seven clinical stroke hospital units, covering all stroke patients within the geographically defined region. The cohort has been described in more detail elsewhere.[19,20] Every second month, new patients were identified in the Danish Stroke Register (DSR), which is a nationwide initiative to monitor the quality of stroke treatment and care,[22] and participation is mandatory for all Danish departments treating patients for acute stroke. Clinical data are prospectively collected by healthcare professionals using standardized registration forms. The register has been found to be valid and complete regarding patient registration.[23,24] All first time stroke patients younger than 80 years, alive 90 days after the stroke and living in their own home prior to the stroke (n=3221), were included in the study and invited to participate. A flowchart describing the selection of study participants and questionnaires is shown in Figure 1.

Questionnaires
Three months after the stroke, the initial questionnaire including questions on self-rated health (SF-12) was sent to the patient by ordinary mail. Three months later and subsequently every 6 months until 2 years from onset of their stroke the patients were asked to fill in the questionnaires. The questionnaires were mailed according to patient specific schedules based on the exact date of the stroke. Except for the first questionnaire, which was always a paper form, patients could choose between paper and web-versions. In the first questionnaire, patients could indicate that they declined further participation. Non-responders were sent a new questionnaire at the time where the patient was supposed to complete the next questionnaire unless they declined. Such non-responding patients were sent up to three questionnaires over 1.5 years. For analysis, we selected the questionnaires for each patient with the best fit with respect to the five fixed time points at 3, 6, 12, 18, and 24 months. Since 1968, all Danish residents have been assigned a unique civil registry number which is used in all health databases and permits unambiguous record linkage between databases. The Civil Registration System contains information on the civil registry number, name, gender, address, date of birth, and vital status.[25] Information on the address and vital status was collected simultaneously prior to approaching the individual patients.

Short-Form 12
The SF-12 is a generic measure of self-rated health that describes the patients' experiences of function and well-being in physical, mental, and social dimensions of life during the past 4 weeks. The scale has been validated in several groups of patients, also in Denmark, and has shown satisfactory reliability and validity among stroke patients.[26–29] The SF-12 consists of 12 questions that correspond to eight subscales and two summary scales: Physical Component Summary (PCS) and Mental Component Summary (MCS) scores. SF-12 scores are graded from 0–100, with higher scores indicating better health. The summary scores are norm-based with a mean of 50 and the standard deviation (SD) equals 10 in a US population sample.[30] We used the Danish translation of the standard SF-12 version 2.0 with scoring as suggested by Ware et al.[30,31]

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┌─────────────────────────────────────────────────┐
│ First-time stroke patients < 80 years prospectively │
│        identified in the Danish Stroke Register      │
│                    n=4327                            │
└─────────────────────────────────────────────────┘
                          │
                          │      ┌─────────────────────────────────────────┐
                          │      │ Patients excluded (n=1106)              │
                          ├─────▶│ Died within first 3 months n=436        │
                          │      │ Living in nursery home n=373            │
                          │      │ Missing register information n=237      │
                          │      │ Hidden address or emigrated n=60        │
                          │      └─────────────────────────────────────────┘
                          ▼
┌─────────────────────────────────────────────────┐
│         Patients mailed questionnaires               │
│                    n=3221                            │
└─────────────────────────────────────────────────┘
                          │
                          │      ┌─────────────────────────────────────────────────┐
                          │      │ Non-response (n=807)                              │
                          ├─────▶│ Died before responding the first questionnaire n=90│
                          │      │ Non-respondents n=717                             │
                          │      └─────────────────────────────────────────────────┘
                          ▼
┌─────────────────────────────────────────────────┐
│    Patients returning at least one questionnaire     │
│                    n=2414                            │
└─────────────────────────────────────────────────┘
                          │
                          │      ┌─────────────────────────────────────────┐
                          │      │ Analysis 1                              │
                          ├─────▶│ Scores at five fixed time-points        │
                          │      └─────────────────────────────────────────┘
                          ▼
┌─────────────────────────────────────────────────┐
│  Patients returning at least two questionnaires      │
│                    n=1613                            │
└─────────────────────────────────────────────────┘
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                          ▼
┌─────────────────────────────────────────────────┐
│ Analysis 2                                           │
│ Longitudinal mixed-model analysis                    │
└─────────────────────────────────────────────────┘
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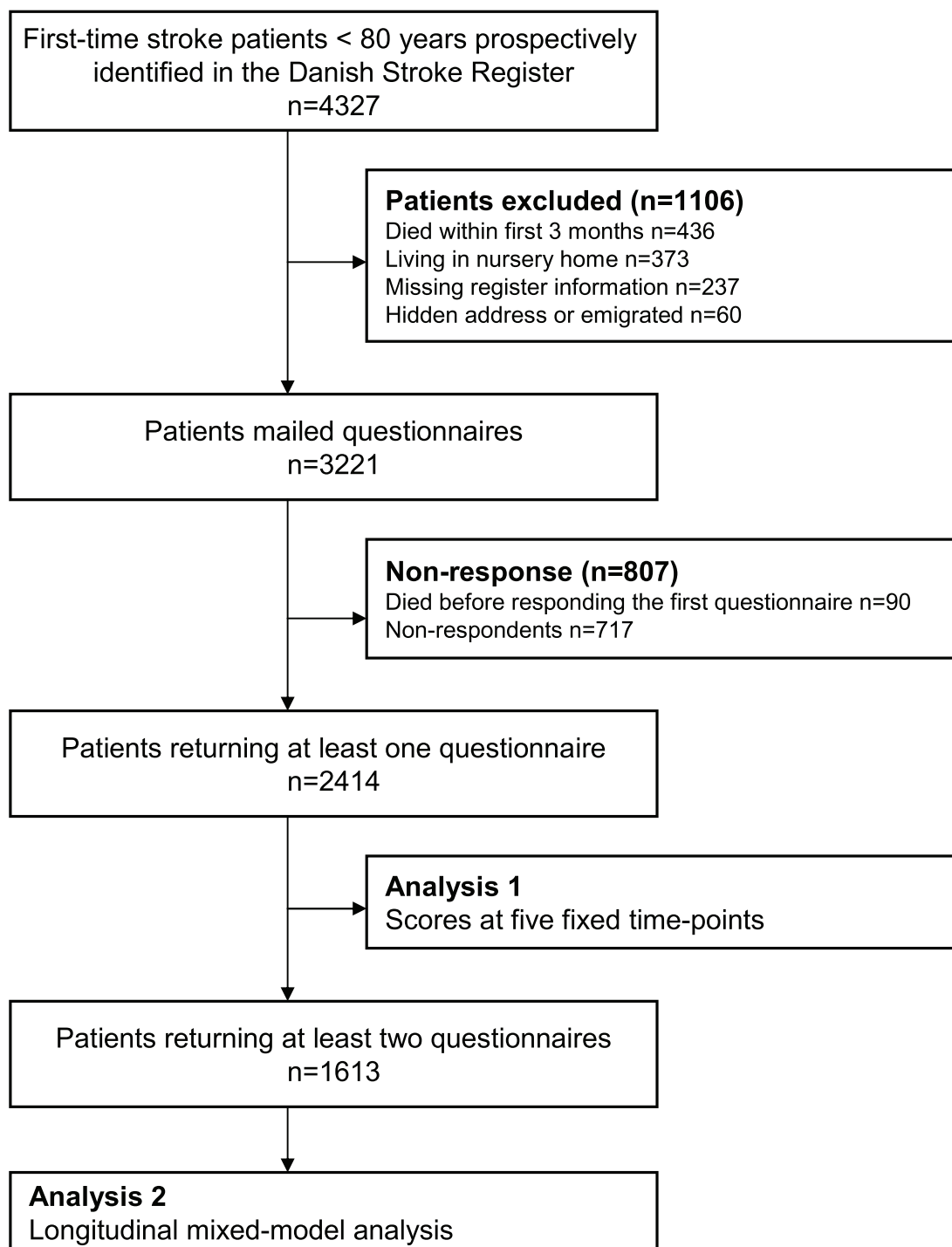
Figure 1 Selection of participants in a cohort of patients for Region Central Denmark suffering first time stroke between October 2008 and January 2012.

Possible Determinant Variables

The following covariates were a priori selected for analysis: gender, age, stroke severity, type of stroke, educational level, and co-morbidity. Information on educational level was collected from questionnaire and categorized as low (less than 10 years education), medium (11–14 years education), and high (more than 15 years of education), as suggested by the International Standard Classification of education.[32] If educational level was missing in the questionnaire, it was estimated based on register information on trade-specific unemployment fund.[33] Information on gender, age, and the possible date of death was obtained from the Danish Civil

Registration System.[25] Age was calculated at the day of the stroke. Information on type of stroke, stroke severity, body mass index (BMI), alcohol consumption, and smoking habits were obtained from the patient's record in the DSR register. Stroke severity was measured at admittance by the Scandinavian Stroke Scale (SSS) and is graded from 0–58 with low scores indicating severe stroke.[34,35] Type of stroke was categorized as ischemic, intracerebral hemorrhage, or unspecified. Charlson Comorbidity Index covers 19 major disease categories in an overall measure of co-morbidity.[36] The index was calculated from the data obtained form of the Danish National Patient Registry.[37]

Statistical Methods

The courses of the SF-12 summary scores were presented graphically, where curves were constructed using Lowess smoothing curves with the default bandwidth of 0.8. In the first analytic approach (Figure 1), we calculated regression based adjusted mean score for MCS and PCS at each of five selected time-point and analyzed the impact of covariates on differences in scores between the levels of the covariates. All responding patients were included in this analysis. Multiple imputations were used to handle missing data. The imputation model was based on register-based data as well as data from the questionnaires and took the individual time course into account. Missing data were imputed 25 times. Analyses were performed both with and without the imputed data and results were supplemented with a sensitivity scenario in which missing measurements were assumed to represent subjects with lower health than esti-mated with the imputation models. Details of the imputation model are given in Supplementary Table I. In a second

longitudinal analytic approach (Figure 1), the overall courses for summary- and sub-scales were analyzed by mixed models and the impact of determinants on the courses of summary scores were evaluated with respect to the same covariates. Time-dependence was evaluated by including time-dependent interaction terms. Patients with at least two questionnaires were included in this analysis. Imputed data were not used in longitudinal analyses based on mixed-models.[38] In both analyses, point estimates of adjusted means were calculated from the multiple regression equa-tion, while the size of 95% confidence intervals and statis-tical tests were based on the standard error of the parameter in question. Statistical analysis were made using Stata 13.0 SE. Estimates were presented with 95% confidence intervals (CI) and P-values below 0.05 were considered statistically significant.

Ethics Approval and Consent to Participate

Participation was voluntary and the study followed the principles of the Declaration of Helsinki and was con-ducted based on approval from the Danish Data Protection Agency journal number 2007–41-0990. According to Danish law, approval by the ethics commit-tee and written informed consent is not required in ques-tionnaire-based and register-based research.

Results

The first questionnaire was mailed to 3,221 patients (Figure 1, Table 1). Ninety patients died before responding to the first questionnaire, and 717 patients declined to participate in the study or remained non-respondent. The

Table 1 Attrition and Response Pattern in a Cohort of Danish First-Time Stroke Patients Alive 90 Days After (N=3,221)

| | Months Since Stroke | | | | |
	3 months	6 months	12 months	18 months	24 months
Cumulative absolute cohort mortality	90	134	185	237	297
Alive in current round	97.2%	95.8%	94.3%	92.6%	90.8%
Send out questionnaires	3,221	2,405	2,196	1,907	1,652
Drop-out	807[a]	198	280	248	211
Attrition	25.1%	8.2%	12.8%	13.0%	12.8%
Active participants	2,414	2,207	1,915	1,659	1,441
Dead[b]	9	11	9	7	n/a
Available for next round	2,405	2,196	1,907	1,652	n/a
Intermittent missing	894	529	403	370	301
Returned questionnaires	1,520	1,678	1,513	1,289	1,140

Notes: [a]9.9% of these patients were alive at 3 months, but died before answering the first questionnaire. [b]Patients who answered the questionnaire in the current round, but died before entering the next round.

remaining patients (n=2,414) all returned one or more questionnaire during the following 24 months. The initial response-rate was 77.1%. Of these patients, 1,613 (66.8%) returned at least two and thus included in the longitudinal analyses. After 24 months, 297 patients had died while 1,140 returned the last questionnaire (Table 1). In total, 7,140 questionnaires were used in the analyses.

The mean age at the date of stroke was 64.5 years (SD=10.9 years). Characteristics of the population are presented in Table 2. More than 60% of the patients were men and ischemic stroke was the most frequent diagnosis.

Course of the SF-12 Summary Component Scores

The measured scores of SF-12 mental component summary (MCS) and physically component summary (PCS) scores are shown in Figure 2. Most patients delivered their responses at the prescribed time-points: 3, 6, 12, 18, and 24 months after the date of their stroke (Figure 2). The MCS score increased with 0.89 points/year (95% CI=0.6– 1.2), while the increase in PCS score did not reach statistical significance (0.13/year; 95% CI=−0.2– 0.5).

The results from the analyses at the fixed time points are presented in Tables 3 and 4, while the results of the longitudinal analyses are shown in Table 5. Similar tables containing 95% confidence intervals are shown in Supplementary Tables II–IV. The determinants for better mental outcome (MCS) were no comorbidity, older age, mild stroke severity, and high educational level. The findings were very similar in the two analytic approaches (Tables 3 and 5). The effect of comorbidity (comorbidity index of 3 or more) and age (70–79 years) showed the strongest effect. The beneficial effect of higher age diminished over time, while the other variables were stable within the 2 years period. With respect to physical health (PCS), the strongest determinants for better physical outcome were mild stroke severity, no comorbidity, higher educational level, and younger age (Tables 4 and 5). The effect of stroke severity and comorbidity both exceeded one half standard deviation (0.78 and 0.60 SD, respectively, Table 5). The negative effect of age increased over time, while the negative effect of stroke severity tended to decrease over the 2 years period (Table 5), but was still the most important determinant for PCS after 24

Table 2 Patient Characteristics of Respondents in a Cohort of Danish Stroke Patients (N=2,414)

|		n	(%)
Gender			
	Female	941	(39%)
	Male	1,473	(61%)
Age			
	18–59	652	(27%)
	60–69	845	(35%)
	70–79	917	(38%)
Marital status			
	Married/cohabiting	1,738	(72%)
	Single	652	(27%)
	Missing	24	(1%)
Education			
	Low (<11 years)	676	(28%)
	Medium (11–14 years)	1,062	(44%)
	High (15+ years)	435	(18%)
	Missing	241	(10%)
Comorbidity			
	Charlson Index 0	1,400	(58%)
	Charlson Index 1–2	966	(40%)
	Charlson Index 3+	48	(2%)
Stroke severity			
	Mild	1,642	(68%)
	Moderate	362	(15%)
	Severe/very severe	241	(10%)
	Missing	169	(7%)
Type of stroke			
	Ischemic	2,101	(87%)
	Intracerebral hemorrhage	216	(9%)
	Unspecified	72	(3%)
	Missing	0	(0%)
Smoking			
	Current	917	(38%)
	Former	652	(27%)
	Never	724	(30%)
	Missing	121	(5%)
Alcohol			
	<14/21 drinks per week	2,052	(85%)
	14/21+ drinks per week	240	(10%)
	Missing	122	(5%)
Body Mass Index			
	<25 kg/m^2	748	(31%)
	25–29 kg/m^2	893	(37%)
	30+ kg/m^2	483	(20%)
	Missing	290	(12%)
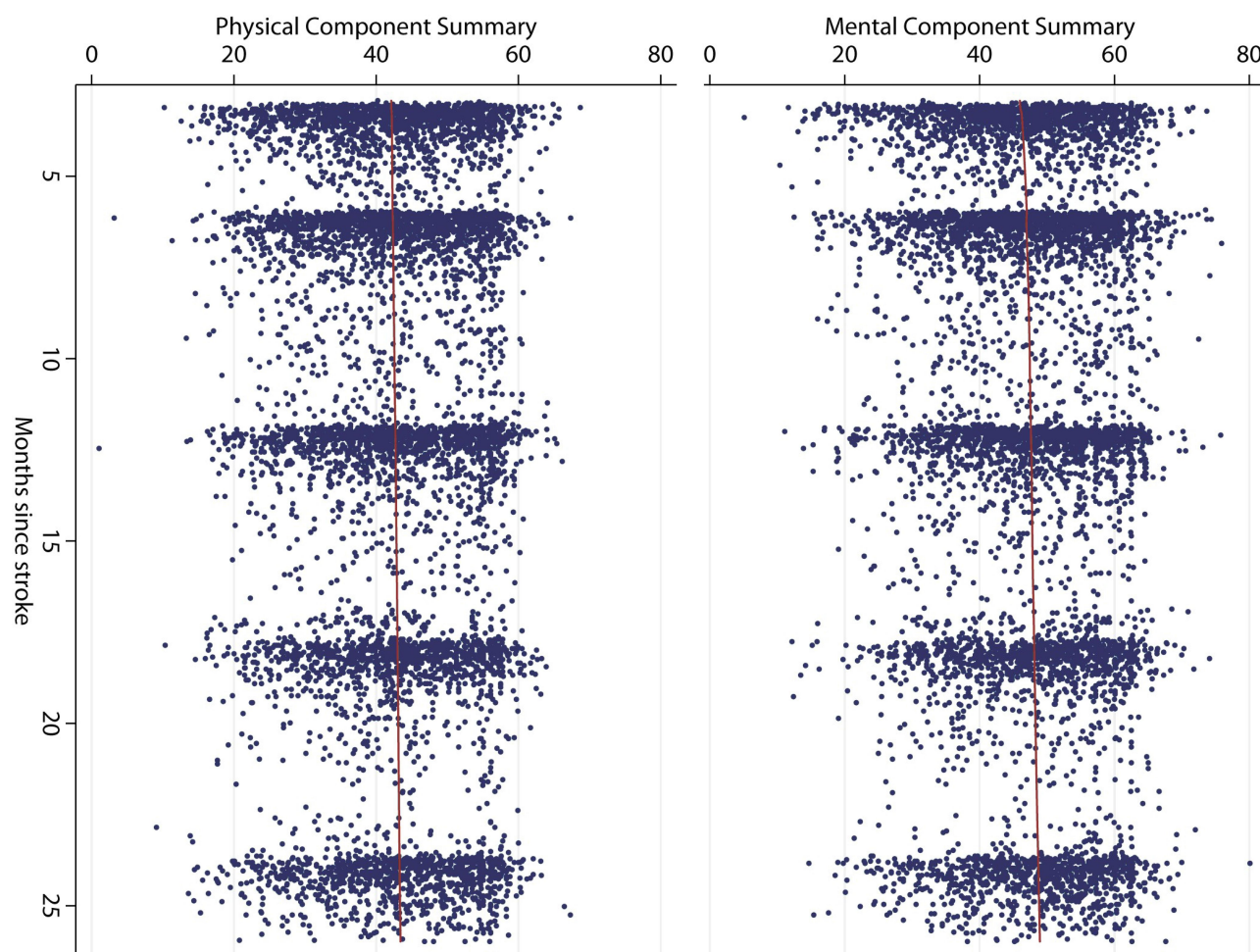
Figure 2 Measurements of Short-Form 12 physical and mental component scores in a cohort of 2,414 Danish first time stroke patients. Lowess smoothing curve bandwidth=0.8.

months (Table 4). The overall strongest effect was found for severe stroke severity after 3 months, where PCS was 0.85 SD below the level among patients with mild stroke severity (Table 4). The type of stroke did not influence the courses of MCS or PCS.

Results from analysis based on imputed data of PCS and MCS scores were similar to those presented in Tables 3 and 4. The results for MCS are presented in Supplementary Table V.

Courses of the SF-12 Sub-Scales

Mean values of the majority of SF-12 sub-scales improved statistical significance during follow-up (Table 6). The largest improvements were found in the domains of physical limitations (Role Physical) and Vitality, with improvements of 2.1 points/year corresponding to nearly one half standard deviation within the 2 year period of follow-up. For these sub-scales the improvements were

most marked during the first 6 months after onset of the stroke (Table 6). No improvements were found in Bodily Pain or Physical Functioning, while the remaining four sub-scales had smaller, but statistically significant, improvements.

Discussion

In a geographically defined population of first-time stroke patients, the mean values of the majority of SF-12 sub-scales and summary scores for mental health improved statistically significantly during a follow-up period of 2 years. The largest improvements were found in the domains of Vitality and Role Physical. For all scales, the improvements were most pronounced during the first 6 months after the stroke. Variables associated with good mental health were male gender, high age, and no comorbidity, while high educational level, young age, mild stroke severity, and no comorbidity were associated with

Table 3 Differences in SF-12 Mental Component Summary (MCS) at Each Point of Follow-Up in a Cohort of 2414 First-Time Danish Stroke Patients

| | Months Since Stroke | | | | | | | | | |
| | 3 | | 6 | | 12 | | 18 | | 24 | |
	Mean	Difference[a]	Mean	Difference[a]	Mean	Difference[a]	Mean	Difference[a]	Mean	Difference[a]
Crude MCS score	45.7		46.7		46.8		47.1		47.7	
Gender										
Female	43.6	Ref	45.2	Ref	45.2	Ref	45.5	Ref	46.4	Ref
Male	47.0	3.2 ***	47.6	2.1 ***	47.9	2.3 ***	48.2	2.3 ***	48.6	1.9 **
Age										
18–59	43.4	Ref	44.6	Ref	44.9	Ref	46.0	Ref	46.1	Ref
60–69	46.7	3.7 ***	47.7	3.4 ***	47.8	3.3 ***	48.0	2.6 ***	48.5	2.8 ***
70–79	46.5	4.3 ***	47.3	3.7 ***	47.2	3.5 ***	47.1	2.4 **	48.3	3.3 ***
Educational level										
Low (<11 years)	45.0	Ref	45.6	Ref	45.9	Ref	45.8	Ref	46.9	Ref
Medium (11–14 years)	45.5	0.4	46.7	1.0	46.6	0.6	47.1	1.1	47.7	0.8
High (14+ years)	47.0	1.6	48.3	2.3 **	48.6	2.3 **	49.2	2.9 ***	49.2	2.0 *
Type of stroke										
Ischemic	46.0	Ref	46.9	Ref	46.9	Ref	47.3	Ref	47.9	Ref
Intracerebral hemorrhage	42.6	−2.6 *	45.5	−0.6	45.3	−0.8	45.5	−1.0	46.3	−0.7
Unspecified	46.4	0.1	44.6	−2.7 *	47.9	0.6	47.1	−0.4	47.4	−0.7
Comorbidity										
Charlson Index 0	46.6	Ref	47.3	Ref	47.7	Ref	48.4	Ref	48.7	Ref
Charlson Index 1–2	45.2	−1.8 **	46.4	−1.3 *	46.2	−1.9 ***	46.1	−2.5 ***	46.7	−2.3 ***
Charlson Index 3+	43.0	−5.0 ***	44.9	−3.4 ***	45.0	−4.2 ***	44.6	−5.6 ***	47.0	−3.7 **
Stroke severity										
Mild	46.4	Ref	47.4	Ref	47.6	Ref	47.9	Ref	48.5	Ref
Moderate	44.6	−1.4	45.5	−1.7 *	45.4	−1.8 **	45.8	−1.7 *	46.3	−1.9 *
Severe/very severe	42.8	−2.8 *	43.6	−3.5 ***	43.8	−3.3 ***	44.1	−3.2 **	45.	−3.0 **

Notes: [a]The differences in scores between levels of categories. Differences were mutually adjusted for all covariates. *P<0.05; **P<0.01; ***P<0.001. 95% CI are displayed in Supplementary Table II.

higher ratings of physical health. Overall, comorbidity and stroke severity were the most important determinants of anunfavorable course of self rated health.

Our study supports previous findings that the progress achieved mentally and physically more than 3 months after the stroke are relatively sparse. Both Haley et al[6], and Suenkeler et al[39] found a decrease in self-rated health in the timespan from 1–4 years after the stroke. Other studies found, as we did, some improvements or steady state in self-rated health in the time after a stroke.[40–42]

Scandinavian Stroke Scale scores typically deteriorate in about 1/3 of patients with intracerebral hemorrhage within the first days.[43] Contrary, some patients with ischemic stroke experience a marked improvement after thrombolytic therapy.[44] We only had access to data on SSS obtained at admission and not at discharge, and for that reason the association between SSS and self-rated health among patients with intracerebral hemorrhage might have been attenuated.

While the majority of the stroke patients were men, female patients rated their mental and physical health significantly lower than men at all times of measurement, most pronounced for mental health. The difference between genders was relatively constant during follow-up, and gender was not a predictor for change, which is consistent with findings in other studies.[6,7,40] However, Muus et al[45] found in a Danish study female patients to recover more slowly than men, and male gender to be a strong determinant for deterioration in

Table 4 Differences in SF-12 Physical Component Summary (PCS) at Each Point of Follow-Up in a Cohort of 2414 First-Time Danish Stroke Patients

	Months Since Stroke									
	3		6		12		18		24	
	Mean	Difference[a]	Mean	Difference[a]	Mean	Difference[a]	Mean	Difference[a]	Mean	Difference[a]
Unadjusted PCS score	41.6		41.9		42.1		42.1		42	
Gender										
Female	40.7	Ref	40.6	Ref	40.3	Ref	40.4	Ref	40.2	Ref
Male	42.2	0.6	42.7	1.3 **	43.2	2.1 ***	43.3	2.0 ***	43.1	2.0 ***
Age										
18–59	43.2	Ref	44.0	Ref	44.5	Ref	44.5	Ref	44.8	Ref
60–69	42.4	−0.1	42.7	−0.5	42.8	−1.1	43.1	−0.7	42.7	−1.5 *
70–79	39.8	−1.6 *	39.6	−2.6 ***	39.7	−3.2 ***	39.5	−3.3 ***	39.1	−4.2 ***
Educational level										
Low (<11 years)	39.3	Ref	39.7	Ref	39.9	Ref	39.8	Ref	39.5	Ref
Medium (11–14 years)	41.9	2.2 ***	42.1	2.0 ***	42.3	1.8 **	42.4	2.0 **	42.2	2.1 ***
High (15+ years)	44.5	4.2 ***	44.9	4.0 ***	44.9	3.7 ***	45.2	4.1 ***	45.1	4.4 ***
Type of stroke										
Ischemic	41.8	Ref	42.0	Ref	42.2	Ref	42.3	Ref	42.1	Ref
Intracerebral hemorrhage	39.9	−0.1	40.1	−0.5	40.7	−0.2	41.1	0.2	40.4	−0.4
Unspecified	41.7	−0.4	42.5	0.3	42.2	−0.4	41.6	−0.8	42.5	0.2
Comorbidity										
Charlson Index 0	43.4	Ref	43.8	Ref	43.8	Ref	44.0	Ref	43.7	Ref
Charlson Index 1–2	40.4	−2.4 ***	40.5	−2.6 ***	40.7	−2.3 ***	40.5	−2.7 ***	40.5	−2.2 ***
Charlson Index 3+	35.8	−6.3 ***	35.6	−6.9 ***	37.6	−5.9 ***	37.6	−6.2 ***	37.6	−5.3 ***
Stroke severity										
Mild	43.5	Ref	43.6	Ref	43.6	Ref	43.6	Ref	43.5	Ref
Moderate	38.2	−4.6 *	38.8	−3,9 ***	39.2	−3,5 ***	39.5	−3,2 ***	39.1	−3,5 ***
Severe/very severe	34.6	−8.5 ***	35.7	−7.3 ***	36.6	−6.5 ***	36.5	−6.5 ***	36.6	−6.2 ***

Notes: [a]The differences in scores between levels of categories. Differences were mutually adjusted for all covariates. *$P<0.05$; **$P<0.01$; ***$P<0.001$. 95% CI are displayed in Supplementary Table III.

HRQoL in comparison with the pre-stroke state. This difference may be due to different ways of measuring self-rated health.

While higher age was associated with better mental health, a negative effect of age was found for physical health. The positive effect on mental health attenuated over time while the negative effect on physical health tended to become stronger. Also in the general population, older age is associated with high mental health and low physical health.[6,31] Similar results in stroke patients have previously been reported.[9,14] We also found higher age associated with less improvement of self-rated health compared to younger patients. Previous studies did not find age associated with the time course of self-rated health after stroke, which may be due to small sample sizes in these studies.[6,7,40,45]

Higher educational level or socioeconomic status has previously been reported to be associated with better self-reported health after stroke.[9] We found a time-stable dose–response pattern in the association between educational level and physical health, where patients with a higher educational level rated their physical health higher.

The high level of comorbidity had a strong and time-stable impact on physical as well as mental health. Most other studies analyzed comorbidity by single diseases and found varying results. We used a systematic and register based method to assess comorbidity, which may explain the stronger effect in this study.

After experiencing a stroke, patients may lower their expectations to the future, which may have influenced the patients rating of own health after stroke. High scores on the SF-12 scale could possibly reflect a response shift, ie,

Table 5 Determinants of Courses of SF-12 Mental and Physical Component Summary (MCS/PCS) in a Cohort of 1613 Danish Stroke Patients

	MCS		PCS	
	Difference[a]	Time dependence[b]	Difference[a]	Time dependence[b]
Gender				
Female	Ref	Ref	Ref	Ref
Male	3.0 ***	−0.03	1.4 *	0.04
Age, years				
18–59	Ref	Ref	Ref	Ref
60–69	3.6 ***	−0.04	−0.2	−0.02
70–79	4.0 ***	−0.08 *	−1.9 **	−0.09 **
Educational level				
Low (<11 years)	Ref	Ref	Ref	Ref
Medium (11–14 years)	0.5	0.01	2.0 **	−0.01
High (14+ years)	1.8 *	0.03	3.8 ***	0.01
Type of stroke				
Ischemic	Ref	Ref	Ref	Ref
Intracerebral hemorrhage	−1.3	0.01	−1.0	0.03
Unspecified	−3.2	0.13	1.3	−0.05
Comorbidity				
Charlson Index 0	Ref	Ref	Ref	Ref
Charlson Index 1–2	−0.6	−0.07 *	−2.1 ***	−0.01
Charlson Index 3+	−3.5 ***	−0.02	−6.0 ***	−0.01
Stroke severity				
Mild	Ref	Ref	Ref	Ref
Moderate	−1.3	−0.06	−4.5 ***	0.07
Severe/very severe	−2.2 *	−0.08	−7.8 ***	0.12 *

Notes: *$P<0.05$; **$P<0.01$; ***$P<0.001$. [a]The differences in scores between levels of categories. Differences were mutually adjusted for all covariates. [b]Interaction term between levels of the covariate and time 95% CI are displayed in Supplementary Table IV.

Table 6 Unadjusted Means (95% CI) of SF-12 Subscales at Each Time Point of Follow-Up in a Cohort of 2414 Danish First-Time Stroke Patients

Months Since Stroke	Physical Functioning (PF)	Role Physical (RP)	Bodily Pain (BP)	General Health (GH)	Vitality (VT)	Social Function (SF)	Role Emotional (RE)	Mental Health (MH)
3	58.2 (56.6–59.7)	51.6 (50.1–53.1)	68.1 (66.5–69.7)	53.2 (51.8–54.3)	40.6 (39.0–41.8)	73.9 (72.2–75.5)	61.8 (60.2–63.4)	66.0 (64.9–67.0)
6	59.4 (57.2–60.9)	54.0 (52.6–55.4)	68.8 (67.4–70.2)	54.2 (53.1–55.4)	42.6 (41.3–43.9)	75.9 (74.6–77.3)	65.0 (63.7–66.4)	67.0 (66.0–68.0)
12	59.1 (57.8–61.0)	55.5 (54.0–57.0)	69.1 (67.6–70.5)	55.3 (54.2–56.4)	42.7 (41.4–44.0)	76.2 (74.9–77.5)	64.7 (63.3–66.2)	68.0 (67.0–69.1)
18	59.4 (57.7–61.1)	56.3 (54.8–57.7)	69.0 (67.4–70.6)	54.7 (53.6–55.9)	44.6 (43.1–46.1)	75.5 (74.1–76.9)	65.2 (63.7–66.7)	68.5 (67.6–69.5)
24	58.7 (56.9–60.4)	56.1 (54.4–57.6)	69.7 (68.2–71.3)	56.2 (55.0–57.5)	44.5 (43.0–46.0)	77.9 (76.4–79.5)	65.6 (64.0–67.2)	69.1 (67.9–70.3)
Increase per year	−0.1 (−1.2;0.9) $P=0.81$	2.1 (1.1;3.2) $P<0.0001$	0.6 (−0.5;1.6) $P=0.29$	1.3 (0.5;2.1) $P<0.01$	2.1 (1.1;3.1) $P<0.0001$	1.5 (0.6;2.5) $P<0.01$	1.5 (0.7;2.2) $P<0.001$	1.7 (0.9;2.5) $P<0.001$

that after a stroke patients lower their expectations, and change their frame of reference to what is good quality-of-life. Previous studies did not find differences in responses when comparing stroke patients to older stroke-free patients, indicating that the change in self-rated health over time among stroke patients was real, rather than a result of response shift.[46,47]

This patient cohort was geographically well defined, was large, and had a long follow-up with a multitude of measurement points and with comprehensive information obtained

from national registries. The study comprised more than 2,000 first time stroke patients and is thus by far the largest cohort study of stroke patients in terms of number of patients as well as the number of measurements. Only two other studies included more than 500 patients,[4,48] with 612 as the largest number of participating patients,[48] and in these studies only two and one measurement points, respectively, were applied. However, some limitations should be considered. We did not have measurements of self-rated health for the first 3 months, and our findings do not apply to stroke patients admitted from nursing homes. Furthermore, we did not include patients over 80 years, accounting for approximately 29% of all acute stroke patients,[49] because we anticipated a low response rate in this group. However, the correlation between age and response rate was weak, so in future studies we recommend to consider a higher age cut-off or to omit any age criterium. We did not send reminders to non-responders because we thought that this may provoke an active decision of not to participate. Instead we send a new short questionnaire after 3 months. This has probably increased the number of participating patients, but also increased the number of missing data in the measure of self-rated health at each time point. Seventy-five percent of patients alive after 3 months returned at least one questionnaire. However, the initial response-rate and the following attrition constitute the main weakness of the study since drop out is likely to be differential. Low and differential participation rates in cohorts of patients with severe chronic is a well known problem. However, results based on the original and the imputed dataset were largely similar, which indicates missing data as a minor problem in this study and the two different analytic approaches we applied to deal with missing data (mixed models and multiple imputation) gave similar results with respect to the determinants.

Conclusion

Stroke is a disease with long-term consequences on a wide range of health aspects. Small improvements in self-rated mental health may be observed during the first 2 years after the stroke. Level as well as course differs between sub-groups, and careful treatment of comorbidity may be an important target with respect to rehabilitation.

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Disclosure

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