Early Supported Discharge after stroke in Bergen

Effects on functional outcome and outcome predictors studied in a three-armed randomised controlled trial comparing rehabilitation in a day unit and in the patients' homes with treatment as usual

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Scientific environment

This thesis is based on the randomised clinical trial "Early Supported Discharge after Stroke in Bergen" (ESD Stroke Bergen), which was initiated by Professor Jan Sture Skouen, Department of Physical Medicine and Rehabilitation, Haukeland University Hospital and Institute for Global Public Health and Primary Care, Physiotherapy Research Group, University of Bergen. The trial was carried out in collaboration between Haukeland University Hospital, the University of Bergen and the Municipality of Bergen from 2008 to 2012.

The supervisors for my scientific work have been Professor Skouen and Professor Halvor Næss, Department of Neurology, Haukeland University Hospital. I have also been a member of the Physiotherapy Research Group at the Institute for Global Public Health and Primary Care, led by Professor Liv Inger Strand.

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Haukeland University Hospital

UNIVERSITY OF BERGEN

BERGEN KOMMUNE

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The Early Supported Discharge after Stroke in Bergen project was based on the establishment of a new rehabilitation chain for stroke patients, reaching from the acute phase in the stroke unit to community rehabilitation, follow-ups and extensive testing throughout. A vast number of persons have therefore been participating at different levels. They are listed in Appendix 2 to this thesis and it has been a pleasure to collaborate with every single one. Thank you all so much!

Three hundred forty-seven patients were recruited to the study and 306 remained for the analyses. I am grateful for their contribution by accepting to participate, being extensively tested, answering many questionnaires and coming to follow-ups.

Professor Jan Sture Skouen MD PhD, research leader at the Department of Physical Medicine and Rehabilitation, Haukeland University Hospital, has been my primary collaborator as well as main supervisor throughout. He conceived the study and has been project leader. I really appreciate his never-ending interest and enthusiasm through the eight years it has taken to carry through this project. My sincere thanks to you, Sture!

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Foreword

I started working at the Department of Neurology, Haukeland University Hospital in 1981. At that time stroke was not a main focus for neurology and neurologists, and most patients were treated at internal medical wards. Also, stroke was a disease without many treatment options. This has changed dramatically during the last 20 years, especially with the introduction of effective treatment options like thrombolysis and, during the last decade, intra-arterial clot extraction procedures. In addition, primary as well as secondary prophylaxis has been improved, systematised and implemented.

In 1993 I changed into working with rehabilitation at the then county specialised institution Nordåstunet. Stroke was always the largest patient group. After the hospital trust reform of 2002, Nordåstunet was reorganised to be an integral part of the recently established Department of Physical Medicine and Rehabilitation at Haukeland University Hospital. Scientific work was planned at the Department from quite early on. Since stroke represented a major patient group, stroke rehabilitation become one important topic for the department's research plans.

I had some research experience from my years at the Department of Neurology, and when I got the opportunity to engage in a major stroke rehabilitation study I immediately accepted this possibility to resume scientific work. My involvement with the ESD Bergen Stroke study started in 2007 and has been on-going since then. I was a full time PhD research fellow for three years (2008-2011) and have been working part-time with the study during the periods before and after. Also my daily work as a senior consultant at the rehabilitation ward concerns stroke rehabilitation.

Working on the ESD Stroke Bergen project has been a long, arduous and challenging journey and I have acquired extensive new knowledge during the process. It is a great satisfaction for me now to be able to present the main results from the study in this thesis!

Bergen, May 2015

List of abbreviations

ADL	Activities of Daily Living
BI	Barthel Index
CT	Computerised Tomography
DPMR	Department of Physical Medicine and Rehabilitation
ESD	Early Supported Discharge
FAC	Functional Ambulation Categories
MMSE	Mini Mental State Examination
MRI	Magnetic Resonance Imaging
mRS	Modified Rankin Scale
NIHSS	New York Institutes of Health Stroke Scale
NRS	Numeric Rating Scale
PASS	Postural Assessment Scale for Stroke
RCT	Randomised Controlled Trial
SHC	Subjective Health Complaints
TIS-modNV	Trunk Impairment Scale-modified Norwegian version
TUG	Timed Up-and-Go
5mTW	5 meter Timed Walk

Abstract

Stroke is a leading cause of lasting disability. Also, the numbers of new strokes as well as persons living with functional disability after stroke are expected to increase further during the coming decades. Efficient and well-structured rehabilitation services are therefore needed. The present thesis describes the implementation of an improved rehabilitation chain for stroke patients based on the Early Supported Discharge (ESD) concept, as well as the results of a randomised controlled trial (RCT) comparing the functional outcomes of two different ESD modalities compared to treatment as usual.

The four essential elements of the two ESD modalities in our study were: (1) as early discharge as possible from institution to the patients' homes, (2) supervision by a hospital-based multidisciplinary coordinating team during the hospital stay and the discharge process, (3) rehabilitation offered by a community-based multidisciplinary health team and (4) out-patient follow-ups 3 and 6 months after the incident stroke. The two ESD modalities differed by the community health team treatment arena: either in a day unit (ESD 1) or in the patient's own home (ESD 2). Altogether 306 stroke patients were included in the study during a three-year period (2008-2011).

The published protocol for the study constitutes Paper 1, whereas the main results of the RCT are reported in Paper 2. The main outcome was modified Rankin Scale (mRS). We generally found somewhat better functional outcome in the ESD 1 and 2 groups compared to the controls, with some significant differences at 3 months, but not at 6 months. There were only slight differences between the two ESD groups. The rather small differences between the intervention groups and the control group may partly be ascribed to the recruitment of fewer participants to the study than planned, thereby reducing the study's statistical power. In addition, stroke treatment including rehabilitation today is of high quality in general, which will tend to minimalize the potential benefit of further service improvement.

In Paper 3 the subgroup of participants discharged directly from the stroke unit to home was studied, 167 patients in all (55% of all participants). This study compared the effects of the three different treatment schemes on balance and walking 3 months after inclusion. No group differences regarding this study's main outcome Postural Assessment Scale for Stroke (PASS) were demonstrated. Analysis of secondary outcomes did, however, show significant differences regarding walking ability (best in the ESD 1 group) and Activities of Daily Living (ADL) (best in the ESD 2 group). These differential effects of the two different ESD modalities may be explained by somewhat differing intervention profiles in the two treatment arenas (day unit or home).

In Paper 4 a systematic exploration of possible predictors of functional outcome was conducted. Thirty baseline variables were analysed using regression analysis with absolute level of functional outcome (mRS at 6 months) and functional change from stable baseline to 6 months (change in mRS) as dependent variables. Stroke severity was the main predictor for mRS at 6 months, but in addition the degree of pre-stroke subjective health complaints strongly predicted a poorer functional outcome. Pre-stroke subjective health complaints also was the only strong predictor for functional change from baseline to 6 months, with higher burden indicating poorer functional improvement. In addition, including subjective health complaints in the final prediction models ameliorated the negative predictive effect of female sex. This indicates that the frequently reported generally poorer functional prognosis for women may be related to their higher burden of subjective health complaints.

In summary, the main RCT demonstrated some significant functional benefit of ESD as compared to treatment as usual at 3 months, but not at 6 months. The effect of the two ESD modalities did not differ. In the subgroup discharged directly to home and evaluated at 3 months some advantages of the ESD modalities concerning walking ability and ADL were demonstrated. In the prediction study stroke severity was the main predictor of functional outcome at 6 months. In addition, pre-stroke subjective health complaints was a strong negative predictor for both absolute functional ability and change from baseline to 6 months.

List of publications

Paper 1

Hofstad H, Næss H, Moe-Nilssen R, Skouen JS.
Early supported discharge after stroke in Bergen (ESD Stroke Bergen): a randomized controlled trial comparing rehabilitation in a day unit or in the patients' homes with conventional treatment.
Int J Stroke. 2013 Oct;8(7):582-587.

Paper 2

Hofstad H, Gjelsvik BE, Næss H, Eide GE, Skouen JS.
Early supported discharge after stroke in Bergen (ESD Stroke Bergen): three and six months results of a randomised controlled trial comparing two early supported discharge schemes with treatment as usual.
BMC Neurol. 2014 Dec 21;14(1):239

Paper 3

Gjelsvik BE, Hofstad H, Smedal T, Eide GE, Næss H, Skouen JS, Frisk B, Daltveit S, Strand LI.
Balance and walking after three different models of stroke rehabilitation: early supported discharge in a day unit or at home, and traditional treatment (control).
BMJ Open. 2014 May 14;4(5):e004358

Paper 4

Hofstad H, Næss H, Gjelsvik BE, Eide GE, Skouen JS.
Cerebrovascular Stroke: Pre-stroke Subjective Health Complaints Predict Functional Outcome Six Months after Stroke.
Submitted to Journal of Stroke and Cerebrovascular Diseases

1. Introduction

This thesis is about rehabilitation after cerebrovascular stroke, exploring the effects of an improved treatment chain based on Early Supported Discharge.

Some decades ago stroke was a disorder with only sparse treatment possibilities. Today acute stroke has evolved into an emergency condition where every minute counts, due to acute treatment options in the form of thrombolysis or intra-arterial clot extraction procedures (1). Most strokes however leave functional deficits on the side of the patient, necessitating subsequent rehabilitation. This rehabilitation has traditionally been delivered within an in-patient institutional setting, often in specialised rehabilitation departments.

This operating mode has, however, been challenged in recent years. The number of stroke patients is high and expected to further rise considerably in the future, due to the anticipated demographic changes in the coming few decades (2). Since the early 1990s an alternative mode of stroke rehabilitation, based on patients living in their own homes while receiving treatment from community service providers, has been described and scientifically studied. This model, termed Early Supported Discharge (ESD), in principle comprises early and coordinated discharge from hospital and rehabilitative treatment provided in the community (3).

The reported results from ESD have been good, meaning equal or better effect than traditional in-patient rehabilitation. The available studies have been summarised in a meta-analysis in Cochrane Reviews, last updated in 2012 (3). In general ESD has led to reduced in-patient time in rehabilitation institutions and a higher degree of independence at follow-up. On the other hand, important issues like the feasibility of ESD in rural areas and more precisely which rehabilitation scheme that is optimal remain unclarified.

The main purpose of the present work was to explore two different models of ESD and to compare the results between them and with the results of rehabilitation as usual in a randomised controlled trial. This paralleled the concomitant and permanent

establishment of a structured rehabilitation chain for stroke patients in our community. Patients with acute stroke were recruited from the stroke unit, Department of Neurology, Haukeland University Hospital, during three years from 2008 to 2011. The two main objectives of the randomised trial were to confirm the superiority of ESD to rehabilitation as usual and to compare the rehabilitation outcome in two different out-patient arenas: in a day unit or in the patients' homes. In addition we wanted to explore which baseline variables that predicted functional outcome 6 months after the incident stroke.

2. Background

2.1 Stroke definition

Cerebrovascular stroke was previously defined according to the World Health Organization (WHO) as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin” (4). Over the years this definition turned increasingly unacceptable, especially since new knowledge demonstrated that permanent cerebral lesions frequently occurred in spite of fully reversible clinical symptoms. In addition, silent cerebral infarcts have been shown to be very common and up to five times as prevalent as clinically manifest strokes (5). This necessitated a new approach to stroke definition, leading to “an updated definition of stroke for the 21st century” published as an expert consensus document in 2013 (6). In this document central nervous system infarction is defined as “brain, spinal cord, or retinal cell death attributable to ischemia, based on neuropathological, neuroimaging, and/or clinical evidence of permanent injury”. It is additionally remarked that “stroke also broadly includes intracerebral hemorrhage and subarachnoid hemorrhage” (6). In this thesis stroke will refer to cerebral infarctions or haemorrhages, but not subarachnoid haemorrhage.

2.2 Stroke incidence and prevalence

Stroke incidence in Norway was reported in 1997 by Ellekjær et al., in a study from Innherred in Central Norway (7). They found a crude incidence rate (first-ever and recurrent stroke) in persons above 15 years of 312 per 100 000, with women more frequently affected (338 per 100 000) than men (285 per 100 000). They later (2007) estimated that the expected annual number of first-ever and recurrent stroke in Norway should be around 11 000 and 3 500, respectively (8). The European incidence of first-ever stroke was estimated in 2009 (9). Six different countries were

evaluated based on national registries, with annual incidences varying from 101 to 239 per 100 000 for men and 63 to 159 per 100 000 for women. The figures for Eastern Europe were more than twice the figures for Southern Europe. These European figures are substantially lower than the estimated incidence in Central Norway referred to above. On the other hand, Næss et al. studied all stroke patients admitted to Haukeland University Hospital during a two year period (2007-2009) and reported a stroke incidence of only 105 per 100 000 in our local area (10). This indicates that the true incidence in Norway may be lower than previously reported.

The stroke lethality has declined strongly during the last decades (8), leading to an increased prevalence of people having suffered a previous stroke. This prevalence has been estimated to 19 per 1000 persons above 20 years in Norway (8;11). All the incidence and prevalence rates quoted above refer to the old WHO stroke definition.

2.3 Stroke treatment and rehabilitation

The essential elements of stroke treatment are acute interventions as early as possible after a verified stroke, additional and supportive treatment during the acute phase, structured rehabilitation, and secondary prophylaxis. Major improvements have been made on these areas during the last few decades, the most important being the acute stroke treatment with thrombolysis (intravenous or, sometimes, intra-arterial) and mechanical clot extraction. This has resulted in reduced persisting disability after stroke (12;13).

To define and characterise rehabilitation The World Health Organization state that (14): “Rehabilitation of people with disabilities is a process aimed at enabling them to reach and maintain their optimal physical, sensory, intellectual, psychological and social functional levels. Rehabilitation provides disabled people with the tools they need to attain independence and self-determination.” This means that the purpose and goal for the stroke rehabilitation process is to enable the patient to live and function

in his or her own home as independently as possible, including participation in social life and, if possible, work.

Rehabilitation performed in a multidisciplinary setting has proven efficacious (15). In this multidisciplinary setting the principles of the International Classification of Functioning, Disability and Health (ICF) are paramount, viewing the patient's condition in a broader context taking into account the disease's consequences for activity and participation as well as personal and contextual factors, in addition to the effects of the stroke itself (16). Stroke rehabilitation today is multi-modal, has proven efficacious and is an integral part of standard stroke treatment (17).

2.4 Demographic challenges in stroke rehabilitation

Stroke, and in particular ischemic stroke, is a strongly age-dependent disease, with a sharply increasing incidence with age (18). This effect, combined with an expected demographic shift with increasing mean age of the population and an especially strong increase in the number of persons within the upper decades, must be expected to result in a continued marked increase in stroke incidence also in the decades to come (2). In addition, the mortality from stroke has been steadily declining for a century and still is (19), and one therefore also has to expect a further increase in the number of people living with lasting disability after stroke. This also means a high and increasing rehabilitation demand in the future.

2.5 Early supported discharge after stroke

The traditional rehabilitation setting for stroke patients has been within departments and institutions, mostly in the specialist healthcare, with the patients being admitted for the rehabilitation period and not being discharged to home for a considerable time period after the stroke. The concept of Early Supported Discharge (ESD) was

introduced into stroke rehabilitation between 1990 and 2000, both internationally and in Norway.

The first ESD study was conducted by Rudd et al. in London, UK, during the period 1993 to 1995 (20). Three hundred thirty-one stroke patients were randomised to either conventional care or early discharge from hospital to specialist community rehabilitation. No significant difference in functional outcome was found, but the time spent in hospital was markedly reduced in the community therapy group (from 18 to 12 days). The authors concluded that early discharge with community rehabilitation was feasible, clinically as effective as conventional care, acceptable to the patients, and with potential for a considerable reduction in the use of hospital beds (20).

After this first publication several more studies based on the concept of Early Supported Discharge were reported during the following decade, and with continued encouraging results (21-30). One of these trials was carried out in Stockholm, Sweden, as early as 1993-96, and with repeated follow-up evaluations at 3, 6 and 12 months (24;31;32). The results in general indicated no less treatment benefit in the ESD group, but there also were several minor findings indicating an advantage for this group. In addition, the length of initial hospital stay was substantially reduced (from 29 to 14 days).

Early Supported Discharge has previously also been investigated in Norway (25-27;30). A large randomised study was conducted in Trondheim during 1995 to 1998 and recruited 320 stroke patients (26). These patients were randomised to either ESD or ordinary care. The main outcomes in the study were modified Rankin Scale (mRS) and Barthel Index (BI) 6 months after inclusion, and the analyses showed a definite benefit of ESD with increased independence and markedly reduced in-patient time (19 days vs. 31 days in the control group) (26). Also at one year follow-up the patients in the intervention group were significantly more frequently independent (33), and five years after inclusion there still was a trend (34).

In another Norwegian study Bautz-Holter et al. randomised 82 stroke patients to either ESD or conventional rehabilitation. They found no clear differences between the groups, but indications that ESD might have additional benefits. The in-patient time was reduced by nine days (27). The possible effect of ESD in a rural setting was explored in a study by Askim et al. who compared ESD and ordinary service in a limited number of patients living in three municipalities near Trondheim (30). No difference in functional outcome one year after the stroke was seen, but a trend towards better quality of life in the ESD group was demonstrated.

A systematic review from the Cochrane Collaboration was issued in 2005, based on 11 randomised trials comprising 1597 patients (35). Trials evaluating the effect of accelerated discharge with provision of additional community support were included. The main conclusions were that ESD reduced dependency and institutionalisation, in addition to markedly reducing days spent in hospital. Services using a coordinated ESD team seemed to be most beneficial. Also, the need for more research to define the essential characteristics of effective ESD services was pointed at, as well as the potential role of ESD in rural areas. This Cochrane review was later updated in 2012 (3). Three new trials were incorporated increasing the number of patients to 1957, but the conclusions from the previous report were not changed.

The Cochrane review includes one more Norwegian study, published by Rønning and Guldvog in 1998 (25). Two rehabilitation modalities were compared in a randomised trial, but none of them can be characterised as Early Supported Discharge since one was sub-acute rehabilitation in a hospital rehabilitation unit and the other was standard rehabilitation in the community. The best outcome was seen in the hospital group. In the 2012 version of the Cochrane report the authors acknowledged that the inclusion of this study had been criticised (3). At the same time a consensus covering essential elements in ESD was reached among 10 ESD trialists, following a modified Delphi approach. The consensus document is published and contains statements regarding team composition, team work model, intervention, and success (36).

The studies included in the Cochrane report were generally conducted some time ago (many 15-20 years before today). Acute stroke treatment, primary and secondary stroke prophylaxis as well as rehabilitation have improved considerably during these years, and one could reasonably question whether the beneficial effects on outcome would still be obtainable today.

On this multifaceted background – both demographic demands, paucity of knowledge about the essential elements of ESD and the time passed since most of the previous studies – we wanted to establish and investigate scientifically a new and improved rehabilitation chain for stroke patients in our local community, based on the concept of Early Supported Discharge.

2.6 Organisational levels of healthcare

The Norwegian healthcare system is organised into two different levels: the community healthcare, including municipal institutions and health care personnel, and the specialist healthcare including hospitals and privately owned institutions. In Norway both healthcare levels carry a responsibility for rehabilitation, and both levels had to be participating in the planned project. Our local municipality, the Municipality of Bergen, at the same time worked on improving their community rehabilitation competence and capacity, and this led to a fruitful collaboration between Haukeland University Hospital (Department of Physical Medicine and Rehabilitation and Department of Neurology), the Municipality of Bergen and the University of Bergen. The project Early Supported Discharge after Stroke in Bergen (short form: ESD Stroke Bergen and in Norwegian: “Slagbehandlingskjeden – Bergen”) was established. This project mostly constituted a scientific research project when viewed from the specialist healthcare position, while at the same time being a developmental project from the point of view of the municipality.

In 2012 the so-called Cooperation Reform was established in Norway (37), in order to increase the efficiency of the healthcare system by emphasising and further

defining the responsibility of both healthcare levels. This obviously necessitated an improved cooperation between the levels. The introduction of this reform coincided with the last period of our ESD research project and the Municipality of Bergen's developmental project.

3. Objectives and hypotheses

The ESD Stroke Bergen study was established with a dual goal. The main objective was to study the effects of two different models of ESD applied to a stroke population from Bergen, and this constituted the scientific research project. Concomitantly with this, and necessary for the research project to be realised, an Early Supported Discharge service for stroke patients in Bergen was established. This constituted the developmental project.

The research project had three main objectives. First we wanted to compare the results of rehabilitation based on the ESD concept with the results of rehabilitation "as usual", and secondly we wanted to investigate the effect of ESD community treatment given in two different settings; either in a day unit or in the patients' homes. The third objective was to explore which variables relating to the patients' life and health before the stroke or to the stroke itself that predicted functional outcome 6 months after the stroke.

Effects of rehabilitation are demanding to study. Patients improve naturally as the disease process heals and it is therefore difficult to discriminate natural healing from more specific treatment effects. The research design of choice in this situation is a randomised controlled trial (RCT), comparing the effects of different treatment modalities in patients randomly allocated to his or her treatment group.

To explore the effects of Early Supported Discharge we therefore designed an RCT with two different ESD arms and one control arm. The null hypothesis for the first research objective was that ESD does not improve functional outcome, and the null hypothesis for the second objective was that day unit and home rehabilitation are equally effective. For the study of possible outcome predictors we used logistic regression analyses.

An integral part of the ESD Bergen Stroke project was the establishment of an improved rehabilitation chain for stroke patients, extending from the admission to the

stroke unit to the delivery of stroke rehabilitation in the community. To study and evaluate this process we approached the Uni Research Rokkan Centre with the request for an organisational study concerning the planning and implementation of the rehabilitation chain. We have also cooperated with a health economist in order to obtain cost analyses relating to the different treatment arms, and a neuropsychological follow-up one year after inclusion has been planned and carried out. These further scientific approaches to the ESD Bergen Stroke study are, however, not the focus of this thesis.

4. Patients and methods

4.1 Study design and organisation

The ESD Stroke Bergen study was organised as a randomised controlled trial with two intervention arms and one control arm, and registered in ClinicalTrials.gov. with registration number NCT00771771. Patients were included in the study shortly after admission to the stroke unit, Haukeland University Hospital, and followed for 6 months after inclusion. They were extensively examined and tested at baseline and 3 and 6 months after inclusion. The project was supervised by a steering group with representatives from the involved parties in addition to the project leader. The overall structure of the study is depicted in Figure 1.

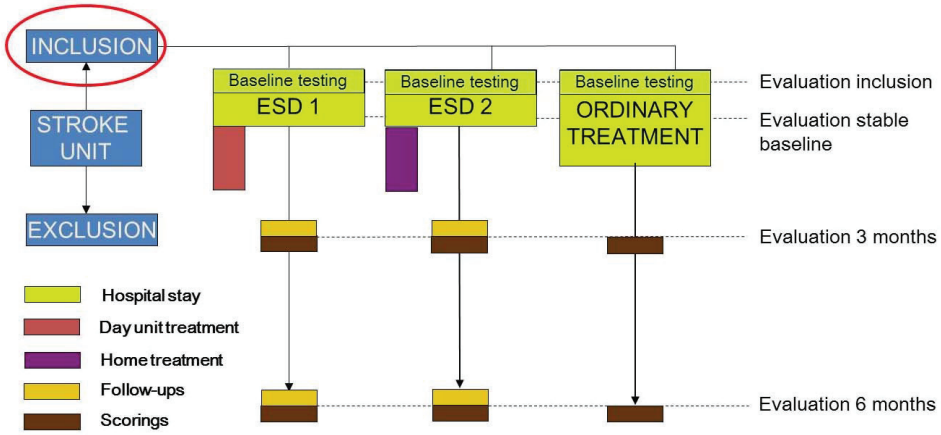

Figure 1 Overview of patient flow and time frame for scorings

4.2 Study population

All patients admitted to the stroke unit with suspected ischaemic or haemorrhagic stroke (but not subarachnoid haemorrhage) during the period 8 December 2008 to 21 December 2011 were assessed for inclusion eligibility following specific inclusion

and exclusion criteria as listed in Table 1. The inclusion was halted during Easter, summer and Christmas holiday periods.

Table 1 Inclusion and exclusion criteria

Inclusion criteria
Patient home-dwelling and living in the Municipality of Bergen
Recent stroke verified by CT or MRI
Inclusion within one to seven days after symptom onset
Inclusion within six hours to five days after admission to stroke unit
NIHSS score 2-26 at inclusion, or mRS score 2 or higher
Patient awake and able to consent; if not consent must be obtained by next-of-kin
No age limit
Exclusion criteria
Serious psychiatric disorder
Alcohol or substance abuse
Other serious conditions interfering with subsequent rehabilitation process
Insufficient knowledge of the Norwegian language pre-stroke

The patients or their relatives if the patient was unable to understand information and make a decision were approached by a designated nurse working in the stroke unit who informed them about the study and asked whether they would participate. The study information was presented according to a template for participation information and consent from the Western Norway Regional Committee for Medical Research Ethics. The participant (or next-of-kin, if the patient was unable to) then signed the informed consent form (see Appendix 1).

The participants were randomised according to a data-generated randomisation list with blocks of six patients, two allocated to each of the three arms in one block. This list was not available in the stroke unit and was confined to a study coordinator at the Department of Physical Medicine and Rehabilitation (DPMR). The patients were allocated to their randomisation arm according to the order in which they were included by the stroke unit recruiting nurse.

4.3 Description of study arms and interventions

The patients were randomised to one of two different Early Supported Discharge modalities (ESD 1 and ESD 2) or a control arm which received treatment and rehabilitation as usual. The intervention arms rehabilitation was based on four principles:

1. The patients should be discharged from the stroke unit (or from additional institutional stay, if necessary) to their homes as early as possible, based on a professional judgement of their functional status. As a rule-of-thumb, discharge home was done when the patient was able to go to the toilet unassisted, and modified by the available degree of next-of-kin support in the home.

2. Immediately after randomisation the patients in the two intervention arms were approached by a member of a multidisciplinary coordinating team. From then on this team member served as the patient's contact person, in particular participating in the discharge process from institution to home. This coordinating team, based in DPMR, consisted of a physiotherapist, an occupational therapist and a nurse. The members of this team did mostly not work profession-specific, but supervised the patients during the stay in hospital and the first period thereafter. They arranged home visits and transfer meetings with the municipal level and secured transfer of clinical information between the two healthcare levels.

3. After discharge from hospital the patients were served by a community-based multidisciplinary health team. This team was the provider of rehabilitation after discharge and also consisted of a physiotherapist, an occupational therapist and a nurse. The team cooperated closely with the hospital-based coordinating team during the discharge process and each of the team members provided profession-specific rehabilitation during the first five weeks after the discharge.

4. All patients were offered follow-ups at the DPMR out-patient clinic 3 and 6 months after inclusion into the study. At these follow-ups they were evaluated clinically by the study physician (the author of this thesis) and they met the

coordinating team member who had been their contact person in the acute phase. During these follow-ups multiple aspects of their situation were discussed and they had ample time for questions.

Neuropsychologist, speech therapist and social worker were not regularly involved, but were available according to need.

The difference between the two ESD modalities was the treatment arena: either at a community day unit (ESD 1) or in the patient's home (ESD 2). Patients in the ESD 1 group had to transfer to the day unit for treatment, while the members of the community health team travelled to the patients' homes in ESD 2. For both groups the duration of treatment was up to four hours a day for five weeks. Many patients, however, received less treatment. The treatment week was organised with three days being directly supervised by the community health team and the remaining two working days for self-training according to instructions by the team.

In order to be able to estimate the amount of treatment received by the participants after discharge home, a form was constructed for self-report on training activities. Participants in the control group were asked to fill in this form from discharge onwards, while ESD 1 and ESD 2 participants were asked to do so during the period following treatment by the community health team. All patients were also asked to fill in a similar form regarding health care contacts and health care received in general.

4.4 Assessments and scorings

Extensive clinical information regarding the patients' acute stroke and comorbidities as well as some demographic variables were entered into the Bergen NORSTROKE Registry database (38) in accordance with the stroke unit's standard procedures. In addition several examinations and scorings specific for the ESD Stroke Bergen study were performed at baseline, either as soon as possible after admission or at stable

baseline (day 7 or earlier if discharged before day 7), and after 3 and 6 months (Table 2).

Table 2 Time frame of scoring instruments used in the ESD Stroke Bergen study

Instrument*	inclusion	stable baseline	3 months	6 months
NIHSS	x	x	x	x
PASS	x		x	x
TIS-modNV	x		x	x
5mTW	x		x	x
TUG	x		x	x
FAC	x		x	x
NRS	x		x	x
MMSE	x			
SHC	x			
mRS		x	x	x
BI		x	x	x
Patient satisfaction			x	x

*Abbreviations: see following paragraphs

National Institutes of Health Stroke Scale (NIHSS) is a systematic assessment tool which provides a semi-quantitative measure of stroke-related neurologic deficit. In this study a 13-item Norwegian version assessing motor function on the affected side only (score 0-34) was used (39).

Postural Assessment Scale for Stroke (PASS) evaluates the patient's degree of postural control during positional changes (40). PASS contains 12 items, with a score range from 0 to 36.

Trunk Impairment Scale-modified Norwegian version (TIS-modNV) evaluates trunk control in sitting (41). The scale consists of six ordinal items and is a modification of the Trunk Impairment Scale originally described by Verheyden et al. in 2004 (42).

Five meter Timed Walk (5mTW) is a test of walking speed (43). The patients were instructed to walk at the most comfortable speed and a 1-2 meter acceleration and deceleration phase was used.

Timed Up-and-Go (TUG) measures the time needed to rise from a chair, walk three metres, turn around and return to sitting position in the chair (44).

Functional Ambulation Categories (FAC) categorises the patient's walking ability in relation to six levels of physical support (45).

Numeric Rating Scales (NRS) express the patient's self-evaluation of stroke-related problems with walking, balance, coping with Activities of Daily Living (ADL), safety in physical activity, pain, and tiredness on an 11-level scale from 0 to 10 (46).

Mini-Mental State Examination (MMSE) is a brief 30-point questionnaire used to screen cognitive function (47).

Subjective health complaints (SHC) were evaluated using the Subjective Health Complaint Inventory of Eriksen et al. (48). Briefly, the respondents rate their subjective discomfort relating to 29 different bodily or psychological symptoms on a 4-point Likert scale from 0 to 3. These symptoms are categorised as belonging to one of five different subscales: musculoskeletal pain (headache, neck pain, upper back pain, low back pain, arm pain, shoulder pain, migraine, and leg pain during physical activity), pseudoneurology (extra heartbeats, heat flushes, sleep problems, tiredness, dizziness, anxiety, and sadness/depression), gastrointestinal problems (heartburn, stomach discomfort, ulcer/non-ulcer dyspepsia, stomach pain, gas discomfort, diarrhoea, and obstipation), allergy (asthma, breathing difficulties, eczema, allergy and chest pain), and flu (cold/flu and coughing).

Modified Rankin Scale (mRS) evaluates the patient's ADL competency in seven levels (0-6) where score 0-2 signifies independence (49;50)

Barthel ADL Index (BI) assesses the patient's ADL function and mobility, in increments of 5 points on a 0 to 100 scale (51).

Patient satisfaction was rated on a 5-point Likert scale, ranging from 1: content to 5: discontent.

Baseline scorings were performed within 1-2 days after admission and before randomisation, except for BI and mRS which were scored on day 7 or earlier if the patient was dismissed from the stroke unit before that. Randomisation group was not

known to the assessors. Scorings at 3 and 6 months were generally performed associated with the corresponding out-patient control for the ESD 1 and 2 groups, while the patients in the control group were seen only by the test personnel. All participants were told not to reveal their group allocation to the testers. Physical tests were performed by a small group of trained physiotherapists, whereas almost all assessments of NIHSS, mRS, BI and patient satisfaction were undertaken by one specifically trained physiotherapist. All data were entered into a data base (either SPSS [physical test results] or EpiData [all other data]).

4.5 Primary outcome

The primary study outcome for the main RCT (Paper 2) was modified Rankin Scale 6 months after inclusion. This measure is very widely used for assessment of functional outcome and was therefore chosen, thereby also making comparisons with other studies possible. The main outcome for the sub-study in Paper 3 was PASS 3 months after inclusion. The other described scorings at 3 and 6 months served as secondary outcomes.

4.6 Sample size estimation

During the preparation of the study the number of included patients was expected to be substantially higher than what we achieved at completion. The estimated sample size was therefore changed under way, ending on expected 350 participants when Paper 1 was submitted. The power calculation for the main RCT (Paper 2) was based on the results from the Trondheim study during 1995-98, which showed a very clear benefit from ESD (26). Dividing the participants into three groups and assuming the same benefit from belonging to one of the intervention groups as in the Trondheim study, a power of 73% (one-sided analysis) to demonstrate a statistically significant difference between the groups for the main outcome mRS was calculated.

4.7 Statistical analyses

Since the main outcome mRS is an ordered parameter non-parametric tests were used for the group comparisons in the main RCT (Paper 2). In Paper 3 the analyses were performed using parametric or non-parametric tests as appropriate depending on the outcome. All analyses were done as intention-to-treat and no imputation of missing data was made. In Paper 4 ordered regression analysis was used.

The statistical programmes package Stata/SE 13.1 for Windows (StataCorp LP, Texas 77845, USA) was used for all data analysis in Papers 2 and 4, whereas the programmes package SPSS V.21 (SPSS Inc., Chicago, Illinois, USA) was used in Paper 3. A qualified statistician (Professor Geir Egil Eide; co-author of papers 2-4) was consulted throughout the study. The statistician was not involved in the data collection or in the treatment process.

4.8 Ethical considerations

Patients in the acute phase after stroke constitute a vulnerable group, amidst a critical health situation and sometimes not able to neither understand information given nor respond adequately to it. In such cases the patients' next-of-kin were asked to decide on behalf of the patient, which later had to confirm the participation if able to do so. Written information and consent were used (see Appendix 1). The patients could withdraw from the study at any time.

During the preparation of the study we regarded it essential that the rehabilitation received by the patients in the intervention arms was at least as effective as usual practice. Discharge to home as early as possible was an important element of the ESD concept, but this should not be done against the will of the patient or next-of-kin, or if otherwise not recommendable from a medical point of view. These specific points as well as the study in general were approved by the Western Norway Regional

Committee for Medical Research Ethics and by the Norwegian Social Science Data Services.

5. Summary of results

5.1 Paper 1

Paper 1 is the published version of the study protocol and therefore does not contain any study results. The essential elements of this protocol have been described in Part 4 of this thesis and will be only briefly summarised here.

To meet the need for increased stroke rehabilitation due to demographic changes with an increased number of old people and a disproportionally larger frequency of stroke, improved stroke rehabilitation based on the ESD concept has been explored and studied since the first half of the 1990s. We designed a three-armed RCT to study the effects of ESD in our community, in close cooperation with the Municipality of Bergen who, on their side, planned a developmental project aiming at improved community rehabilitation. An improved rehabilitation treatment chain was thus constructed, based on four principles: services from a hospital-based multidisciplinary coordinating team from soon after admission, discharge as early as possible from institution to home, services from a community-based multidisciplinary health team from soon after discharge and during the first five weeks thereafter, and out-patient follow-ups at 3 and 6 months.

An extensive array of examinations and scorings was scheduled for performance at baseline, 3, 6, 12 and 24 months (Paper 1, Table 2). Modified Rankin Scale at 6 months was decided upon as the main outcome measure for the RCT trial. The results from evaluations at 12 and 24 months are not reported in this thesis.

5.2 Paper 2

In this paper the main results of the RCT are presented. The flow diagram for eligibility assessment, exclusion, randomisation, intervention received and retest compliance/drop-out is shown in Figure 2.

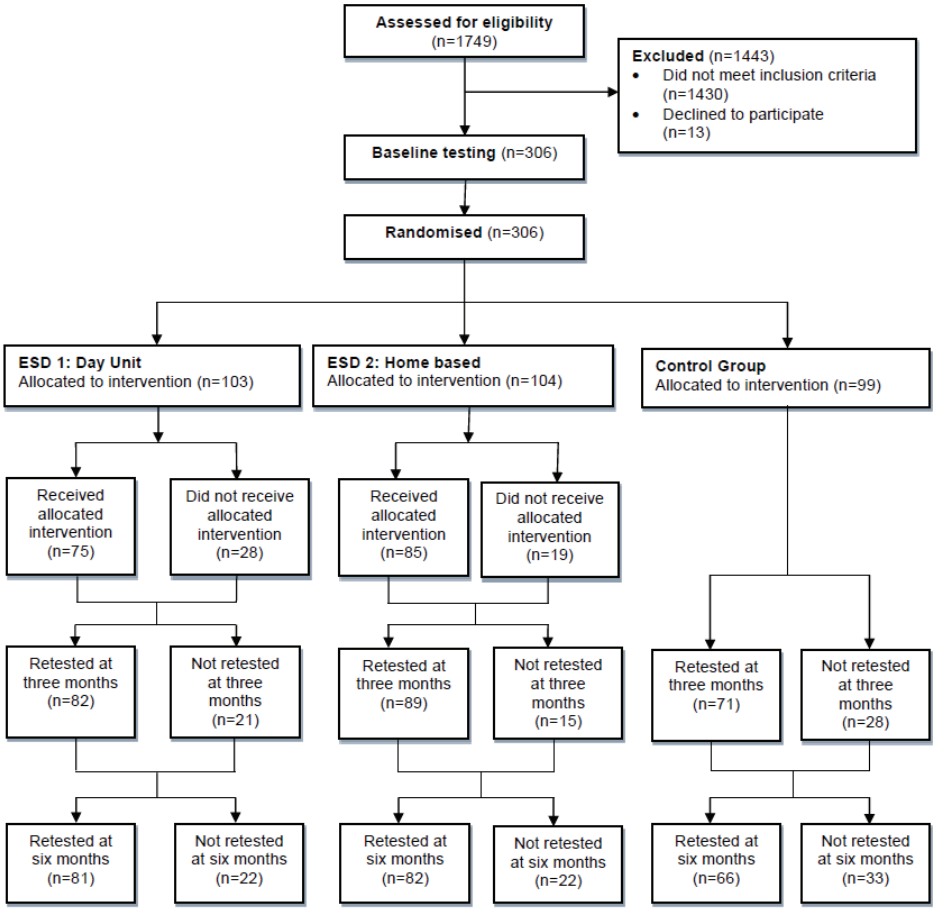

Figure 2 CONSORT flow-diagram showing patient flow from initial assessment for inclusion to 6 months retesting

Three hundred six patients were included, with a mean age of 69.6 years for men (n=169) and 75.6 years for women (n=137). There were no statistically significant differences at baseline between the three randomisation groups, but the women in the control group tended to be older (78.8 years vs. 72.2 for ESD 1 and 75.7 for ESD 2) (Paper 2, Table 1). Recruiting finally 306 patients instead of the intended 350 reduced the power of the study from 73% to 68%.

73% of the ESD 1 patients and 82% of ESD 2 patients received the allocated treatment. The overall drop-out rate at 3 and 6 months was 21% and 25%, varying between the groups with 20%/21% for ESD 1, 14%/21% for ESD 2 and 28%/33% in the control group.

The main outcome mRS was scored at 3 and 6 months and mean mRS scores as well as change scores from baseline were reported. There was generally lower (better) mRS scores in the intervention groups (ESD 1 and ESD 2) compared to the control group, but the differences were not statistically significant (Paper 2, Table 2). The difference in change score from baseline to 3 months, however, approached significance (p=0.063). Within-group analyses from baseline to 3 months showed significant improvement for the ESD 1 (p=0.042) and ESD 2 groups (p=0.001), but no significant change for the control group. Comparisons between men and women showed a statistically highly significant better improvement of mRS in the men at both 3 and 6 months (Paper 2, Table 2).

In another approach the mRS scores were dichotomised to functional independence (≤2) or dependence (>2). With this approach there was a trend towards more patients being independent in the two intervention groups pooled together than in the control group at 3 months (p=0.086) and 6 months (p=0.122). In addition, mRS change scores from baseline to 3 months were significantly larger in the intervention groups pooled together than in the controls (p=0.049). At 6 months there was no difference (Paper 2, Table 3).

For the outcomes BI, NIHSS and patient satisfaction there were no significant differences between the three arms at 3 and 6 months, but a trend towards better patient satisfaction at 3 months (p=0.115) (Paper 2, Table 2).

We also performed two different subgroup analyses. In the first of these the patients were divided according to discharge destination (home, municipal institution or DPMR). This analysis demonstrated a significant difference between the three arms at 3 and 6 months for patients discharged to DPMR, with better mRS in the ESD 1

and ESD 2 groups than in the control arm (p=0.041 and p=0.037, respectively) (Paper 2, Table 4).

In the second subgroup analysis the patients were divided into three groups, as equal in number as possible, according to their last baseline NIHSS score. The groups were NIHSS=0-1 (n=88), NIHSS=2-4 (n=130) and NIHSS ≥5 (n=86). There were statistically significant differences at 6 months for the lowest NIHSS group with ESD 1 having the lowest (best) mRS score (p=0.016) and for the medium group with ESD 2 scoring best (p=0.049). For the most affected NIHSS group there were no significant differences (Paper 2, Table 5).

In Paper 2 we finally looked for differences between the study arms regarding discharge destination, days institutionalised from stroke to first discharge to home and the total time spent in institution (stroke unit, DPMR, municipal institution, or other) during the first 6 months. No significant differences were seen (Paper 2, Table 6).

5.3 Paper 3

The purpose of Paper 3 was to explore the effects of the three different rehabilitation schemes on balance and walking. A subset of the total RCT study population was examined, defined as the participants who were tested at baseline with the balance inventory Postural Assessment Scale for Stroke (PASS) (40) and discharged directly from the stroke unit to home, 167 patients in all. There were no statistically significant differences between the three randomisation arms at baseline.

The primary outcome in the Paper 3 study was PASS, while secondary outcomes were Trunk Impairment Scale-modified Norwegian version (TIS-modNV) (41), Timed Up-and-Go (TUG) (44), Functional Ambulation Categories (FAC) (45), 5 meter Timed Walk (5mTW) (43), and self-report on problems with walking, balance, activities of daily living (ADL), physical activity, pain and tiredness using numeric rating scales (46). Loss to follow-up was 62 patients (37%), and baseline scorings on

PASS, Barthel Index, TUG and 5mTW were significantly poorer in the drop-outs compared to the completers (Paper 3, Table 2). Patients completing the study were significantly more frequently living with a partner ($p<0.001$), and significantly fewer of them had had a previous stroke ($p=0.036$) or needed nursing care before the incident stroke ($p=0.034$) (Paper 3, Table 1).

Putative treatment effects in the 105 patients completing the study (63%) were evaluated by comparing change scores from baseline to 3 months for the various outcomes. Analysis of the primary outcome PASS showed no significant difference between the three groups, but there were significant differences for TIS-modNV and self-reported problems with walking and ADL. TIS-modNV improved more in the home rehabilitation (ESD 2) group than in the two other groups ($p=0.044$) (Paper 3, Table 4). This difference was not, however, significant in pairwise analyses with Bonferroni correction of the significance level to 0.0167 for multiple comparisons.

Improvement of self-reported walking problems was significantly different both between the three groups ($p=0.021$) and in the day rehabilitation (ESD 1) group vs. controls in pairwise analysis ($p=0.004$). The third significant difference between the intervention groups concerned self-report on ADL problems ($p=0.016$), where the home rehabilitation (ESD 2) group did better than the controls in pairwise analysis ($p=0.006$) (Paper 3, Table 4). Also, on a group level, the participants in the day unit group as compared to the two other groups improved above clinically important change in walking speed.

Putative predictors of PASS were explored by multiple linear regression. The analyses showed a significant negative effect of increasing age and significant positive effect of higher baseline PASS score, not having had a previous stroke and not having had previous nursing care.

For the 105 patients completing this study the treatment amount personally provided by members of the community health team (three days per week) to the day rehabilitation (ESD 1) and home rehabilitation (ESD 2) groups was calculated, amounting to mean 22.0 hours in the ESD 1 group and 16.6 hours in the ESD 2

group. In addition, the patients were instructed to exercise at home during the last two working days of the week.

5.4 Paper 4

The purpose of paper 4 was to explore the predictive power of various variables relating to the patients' life and health before the stroke or to the stroke itself. The analyses were performed with both mRS at 6 months and mRS change score from stable baseline to 6 months as outcome measure (dependent variable). Thus, the influence of the candidate variables on both absolute functional level at 6 months and the improvement from stable baseline to 6 months was examined.

Thirty candidate variables were selected, 16 of which related to the pre-stroke condition and 14 to the acute stroke period. Since both outcomes were ordinal, mRS with 7 levels (0 to 6) and mRS change with potentially 13 levels (-6 to 6), ordered logistic regression was chosen for the analyses.

mRS at 6 months was registered in 229 of the 306 patients included in the RCT, representing a drop-out rate of 25%. To evaluate whether the 229 completers differed from the 77 drop-outs, all candidate variables were compared between the two groups. Only two variables differed significantly. The greatest difference was seen for Barthel Index (BI) at stable baseline, being (mean) 75.26 in the completers and 83.38 in the drop-outs ($p=0.008$). However, all patients that died during the time period from stable baseline to 6 months were included with the completers since their mRS at 6 months was known (mRS=6), and this accounted for most of the difference. The second variable differing between completers and drop-outs was estimated mRS before the stroke ($p=0.037$), with a higher degree of functional impairment before the stroke among the completers. The candidate variables are listed in Table 1 in Paper 4, showing values for all 306 patients and split between completers and drop-outs.

A limited number of the candidate variables (subjective health complaints, estimated mRS before the stroke, previous migraine, previous depression and Mini Mental State

Examination score at baseline) were introduced during the study period and therefore not registered in a high proportion of the patients. To preserve a high number of observations and thereby the representativeness of the patient sample these variables were therefore not included in the stepwise multivariate regression analyses, but instead added to the final models.

For each of the two outcomes mRS at 6 months and mRS change from stable baseline to 6 months the analyses were performed on the total patient group (infarctions and haemorrhages; n=229) as well as on the infarction subgroup (n=202), leading to a total of four sets of regression analyses. First univariate regression was performed and then fully adjusted multivariate regression. In the third analysis stepwise backward regression was done, leaving out the least significant variable at each step and stopping when all remaining variables showed significance level of 0.05 or better. The exception to this were the variables age and sex, which by choice were kept in all analyses.

In the univariate regression analyses quite many of the candidate variables were predictive of mRS at 6 months in both the total group and the infarction subgroup (Paper 4, Tables 2-3), but only a few predicted the change in mRS from stable baseline to 6 months (Paper 4, Tables 4-5). In the fully adjusted multivariate analyses (all variables included) of both mRS outcomes (score at 6 months and change from baseline to 6 months) many of the significant associations from the univariate analyses disappeared (Paper 4, Tables 2-5).

In the final models elaborated sex, age, previous cerebrovascular disease, previous peripheral artery disease, thrombolysis performed, tube feeding necessary in acute phase, pneumonia in acute phase and leukoaraiosis were predictive for mRS at 6 months, with some differences between the total group and the infarction subgroup (Paper 4, Tables 2-3). In addition, the variable BI at stable baseline was the dominant predictor in all analyses for the outcome mRS at 6 months with $p<0.001$ in all instances. Detailed information regarding these analyses can be seen from Tables 2-3 in Paper 4.

The final models elaborated from the total patient group as well as the infarction subgroup for the outcome mRS change from stable baseline to 6 months showed only sex, previous cerebrovascular disease and tube feeding necessary in acute phase to be significant predictors (Paper 4, Tables 4-5).

Finally we selectively added the variables with fewer observations and therefore left out in the stepwise regression analyses, but with significance in the univariate analyses, to the four different previously elaborated final models. Of these, the variable subjective health complaints was a highly significant predictor both in univariate analysis and when added to each of the final models (Paper 4, Table 6). The significance level for predicting mRS at 6 months was 0.002-0.004, and for predicting mRS change from baseline to 6 months <0.001 in all models. This means that a higher burden of subjective health complaints predicted both poorer functional level at 6 months and less improvement from stable baseline to 6 months.

Adding subjective health complaints to the final models also removed the significant negative prediction of female sex seen in two of the four models. We therefore post hoc analysed subjective health complaints in both men and women, and found a significantly higher load in women (p=0.005). The patient group with subjective health complaints registered was finally compared to the total patient group, with only one variable (urinary incontinence) differing significantly between the groups.

The results of the prediction analyses are tentatively summarised in Table 3, where significant final model predictors for the two different outcomes in the total study population and in the infarction subgroup are indicated.

Table 3 Summary of predictors in final models with significance probability <0.05 for mRS at 6 months or mRS change from stable baseline to 6 months

Predictor	mRS 6 months All patients	mRS 6 months Infarctions only	mRS change All patients	mRS change Infarctions only
Sex (female vs. male)	+*		+*	
Age	+			
Previous cerebrovascular disease	+		+	+
Previous peripheral artery disease	+			
Barthel Index at stable baseline	++	++		
Thrombolysis performed		+		
Tube feeding necessary in acute phase	+	+		+
Pneumonia in acute phase		+		
Leukoaraiosis on CT or MRI		+		
Subjective health complaints	+	+	++	++

Abbreviations: mRS=modified Rankin Scale; CT=Computerised Tomography; MRI=Magnetic Resonance Imaging;
*Predictive power of sex not present when subjective health complaints are included in the final models
+ indicates significance level 0.05-0.001; ++ indicates significance level <0.001

6. Discussion

6.1 General experiences from the ESD Stroke Bergen study

Conducting the present randomised controlled trial was both demanding and led to new insight into the stroke patient population. We soon realised that recruiting the estimated number of patients would be challenging. Many patients are admitted to the stroke unit with suspected cerebrovascular stroke, but without the diagnosis being confirmed. About half of the patients did not live in the Municipality of Bergen. In addition, the inclusion had to be halted during the holiday seasons for practical and logistic reasons. On the other hand, only few eligible patients declined to participate, and the majority were admitted within the time frame set in the inclusion criteria.

Another problem encountered was adherence to the more specific inclusion criteria regarding stroke severity as defined by NIHSS and mRS. When reviewing these parameters some time after inclusion we discovered that a substantial number of the patients did not qualify according to the set criteria and therefore had to be removed from the study population. Since this was a random occurrence, it did not influence the size and equality of the three randomisation groups, but it hampered the power of the study. One reason for these faulty inclusions may be the many different physicians serving the stroke unit during the study period.

We also experienced a habit of especially young stroke patients being routinely referred to further in-patient rehabilitation, despite having a quite moderate neurological dysfunction which was fully compatible with direct discharge to home. This sometimes resulted in expectations from the patients of a hospital stay also when this was not needed or appropriate. This observation indicates that the concept of ESD still was somewhat unfamiliar to some of the stroke unit's treating physicians. In a recent study from Australia the attitudes and beliefs towards an ESD service were explored in an on-line survey (52). Respondents were referrers to rehabilitation as well as service providers, and their answers demonstrated some level of uncertainty

regarding both the intensity of therapy and the capability of an ESD service to deliver specialised rehabilitation.

It was also challenging to obtain good patient compliance regarding the scheduled follow-up scorings and examinations. The appointed study coordinator was responsible for the logistics in this respect and put much effort into both written appointments and telephoning the patients on the day before to reinforce the appointments and assist with necessary transport arrangements. The follow-ups were originally planned to take place at the Department of Physical Medicine and Rehabilitation (DPMR) out-patient clinic, for practical reasons and because the various physical tests should be undertaken at one place according to a standardised procedure. However, we soon realised that this would lead to an unacceptably high drop-out rate. From early on patients not wanting to come to the out-patient clinic therefore were assessed in their homes for the scorings of mRS, BI, NIHSS and patient satisfaction if they consented to that.

Despite these efforts the drop-out rate regarding the main outcome mRS was 21% at 3 months, increasing to 25% at 6 months (see Paper 2). For the physical tests, which could not be performed in the patients' homes, the drop-out rate was substantially higher with 37% at 3 months (see Paper 3). In general, the drop-out rate was markedly higher in the control group, which can be reasonably explained by the control patients not experiencing as close connection with and obligation towards the study as the patients in the two intervention arms.

We routinely asked the patients dropping out for plausible reasons and most answered the question, although they were not obliged to. The reasons very manifold, including poor physical condition, general tiredness, high age, transport problems, not wanting to spend the time necessary, not wanting any more contact with the hospital, not wanting to take time off work, or being on holiday. In addition to the drop-outs some patients had died since inclusion, amounting to 3.6% at 3 months and 5.2% at 6 months. These patients were, however, included in the mRS outcome analyses since

their mRS score necessarily was 6. For analyses of other outcomes deaths contributed to the patient attrition, but only marginally.

Planning the study we wanted to gain information regarding other treatment received by the patients, for the intervention groups regarding the period after finishing the community rehabilitation and for the control group regarding the whole period after discharge from the stroke unit. The participants therefore received designated forms to make notes of such treatment, but these forms were generally not filled in, or very scantily, and not usable for analysis. This is a weakness of the study, although we are generally familiar with what treatment a stroke patient generally receives after discharge. This "treatment as usual" amounts to physiotherapy one or two hours a week in the majority of patients.

In summary, this study was challenging to conduct, studying patients with a serious illness and often with much comorbidity. The participants had to be recruited in the acute phase, when their focus was directed towards their clinical situation, or they were not fully alert necessitating their next-of-kin to receive study information and consent to participation. The follow-ups required the patients to travel twice to the DPMR out-patient clinic. Lastly, the patients were also frequently enrolled in other stroke studies at the Department of Neurology.

6.2 Paper 1

This paper constituted the protocol for the RCT. The two active treatment arms were based on two different variants of ESD, both dependent on a new treatment chain for stroke patient rehabilitation. This treatment chain comprised service from a multidisciplinary coordinating team during the stay in hospital and the first period thereafter, as early as possible discharge to home, and thereafter rehabilitation given by a designated community health team. The fourth basic rehabilitation element in the study was follow-up at 3 and 6 months. Since knowledge about which components of ESD that are important for the positive effect was mostly lacking in

the literature, two different schemes for the community rehabilitative treatment were defined in the way of two different rehabilitation arenas: either in a day unit or in the patients' homes.

This rehabilitation chain thus depended both on the specialist health care (Haukeland University Hospital) and the community health care (Municipality of Bergen), as well as a close and well-functioning collaboration between these two parties. These aspects of the ESD Stroke Bergen study, representing the developmental project, will be discussed here relating to Paper 1.

6.2.1 Establishing the rehabilitation treatment chain

The process of planning and implementing this rehabilitation treatment chain, necessary for the project to be carried out, has been studied and evaluated by researchers from the Uni Research Rokkan Centre. They conducted semi-structured individual and group interviews during 2010 with persons important for the implementation process and presented initial results in a Norwegian-language report in 2012 (53). Presently the observations are being extended to a journal article presenting the results of qualitative data analysis employing verbatim transcription of the interviews followed by qualitative coding and analysis of the contents. Documents and field notes were also processed in this way, all leading to the characterisation of barriers and facilitators for implementation of the new stroke rehabilitation chain (Ludvigsen et al., submitted).

Barriers identified were the complexity of the organisational coordination, unsecure (initially) and complex funding, "multifaceted objects" (meaning the differing positions and interests of the stakeholders towards the project) and the strict target group definition. On the other hand timing of the project, organisational anchoring, information policy and competence of personnel were listed as facilitators (Ludvigsen et al., submitted).

Before recruitment of patients to the project started in December 2008, a pilot study was conducted during the autumn of 2008. Nine patients were included and followed through all phases embraced in the project up to 3 months follow-up. These nine patients and their rehabilitation were studied by Occupational Therapist Bjørg Rene, forming the basis of her master's degree (54).

6.2.2 The multidisciplinary teams

The essential new elements in the rehabilitation chain were the two new teams: the hospital-based multidisciplinary coordinating team and the community-based multidisciplinary health team. Both teams consisted of a physiotherapist, an occupational therapist and a nurse, and both parties, Haukeland University Hospital and the Community of Bergen, created their team de novo.

The main task for the hospital-based multidisciplinary coordinating team was to establish personal contact with the acute stroke patients as soon as possible after inclusion into the study and thereafter stay in close contact with them through the stay in the stroke unit, during the discharge process and until the community health team had taken over as the main service provider. This work was only to a small degree profession-specific, but each of the team members would confer with one or two of the others when needed, according to the specific situation. After the completion of the study the multidisciplinary coordinating team described their experiences in a report (55).

Based on their experiences from the study period the team especially emphasised the importance of several key factors. Close cooperation with the municipal health team around the individual patients was paramount. This included transfer meetings and home-visits to define the patient's functional capacity and needs in his or her home situation, preferably before discharge. The importance of close contact and regular meeting between the two teams was also emphasised. Also the two different team's roles and work towards the patients needed much discussion and clarification. In each

case, one of the team members served as contact person both for the patient and towards the community health team.

A key role for the multidisciplinary coordinating team was to secure the patient transition between the two levels of the healthcare system, i.e. from the hospital to the community, including information to the patient as well as optimal and swift transfer of medical information. The patient's contact person in the team also participated at the 3 and 6 months follow-ups. This was evaluated as very useful, picking up unmet needs as well as responding to the patients' inquiries and need for new information. In general, themes at 3 months follow-up often were within the body structure and function domain of the ICF, whereas at 6 months questions often concerned the activity and participation domains.

The community-based multidisciplinary health team, on the other hand, delivered profession-specific rehabilitation according to common practice, but in a highly multidisciplinary context. The multidisciplinary community health team has also written an extensive report, describing their experiences during the project period and recommending the future direction for rehabilitation outside institution in the Municipality of Bergen (56). One main conclusion in this report, based on the team members' experience, is that all stroke patients are presumed to benefit from the follow-up by a competent community health team the first period after a stroke.

The physiotherapist and occupational therapist in the community team trained with the patients in physical and daily living activities, and they instructed them in self-training. The team's nurse followed the patients on issues like specific medical problems and medication. Therapeutic conversations with emphasis on life adjustment and coping were also important elements of the team's work, and all members of the team received some formal training in cognitive approach during the project period.

The scheduled maximal amount of training given by the community health team was four hours per day for up to five weeks, and with two of the five working days of the week for self-training. When the protocol was drafted this was considered necessary

to reasonably well match the amount of treatment given to patients in specialised full-time rehabilitation units.

The experience from the study period was, however, that the amount of rehabilitative treatment provided by the community team turned out to be markedly lower. There were many reasons for this, ranging from no need (in patients fully recovered) to patients not wanting treatment because they were feeling too tired, or were too busy for it. Many patients wanted or needed some days "off" after discharge from hospital, and they were in such cases allowed up to one week "rest" before the community health team started its work. Another issue complicating the patients' participation according to the protocol was transport. Patients randomised to the ESD 1 arm had to transfer to the community day unit to have their treatment, which was troublesome for some of them (physical problems or economical/logistic issues related to the taxi transfer) and hampered their compliance. This problem obviously did not occur in the ESD 2 group, where the therapists came to the patients' homes.

The amount of treatment actually received by the patients in the two randomisation arms from the community health team was specifically counted in Paper 3, with the results being 16.6 hours for ESD 1 and 22.0 hours for ESD 2. In comparison, the maximal treatment time allowed for per protocol amounts to four hours per day, three days per week for five weeks, totalling 60 hours.

One challenge facing the community health team were patients preferring the treatment mode of the other arm, and especially ESD 1 patients wanting treatment in their own homes. The regimens for each group were, however, followed strictly during the study, with the only exception allowed being one home visit for the ESD 1 group to aid the therapists in their recommendations.

In their report the community health team discusses the project's two rehabilitation arenas in some detail (56). They experienced that day unit treatment allowed for more intensive, structured and varied rehabilitation, and in a more multidisciplinary setting than home rehabilitation. Home rehabilitation, on the other hand, allowed for more specific and task-oriented training as well as better "access" to the patient's next-of-

kin. In addition, home rehabilitation also was preferable for patients not easily able to leave the home.

During the study we strongly felt that it would have been preferable to assign the treatment localisation individually according to the patient's specific needs and wishes, and the team's conclusion on this in their report is in accordance with this. They find that a combination of the two (day unit and home) would be beneficial for the majority of the patients, and perhaps with home rehabilitation initially followed by day unit treatment afterwards. In fact, this mode with both options available has later been adopted by the community health team after completion of the study. In addition, the maximal duration of the team's treatment period has now been extended to three months.

Both the hospital multidisciplinary coordinating team and the community multidisciplinary health team were established de novo at study start. A close cooperation between these teams was an obvious necessity and they established regular meetings where both general issues and particular patients were discussed. In addition, the teams met with both community administrators engaged in the project and the investigators from the hospital 4-6 times a year for general discussions. These meetings were very important for the collaboration between involved parties in the project.

The ESD rehabilitation chain for stroke patients as described in Paper 1 and discussed here was established with intended permanency. The experiences from the study period (2008-2012) were generally very good, demonstrating this to be a feasible working collaboration. During the study period the members of the team gradually increased from three to six persons. After the end of the study period this has been further extended to four different teams of three persons each, with each team serving two of Bergen's eight boroughs. Stroke patients still constitute the core patient group, but patients with traumatic head injury or multiple sclerosis may also be treated in accordance with a planned and controlled extension of disease entities served by the team.

6.3 Paper 2

The results regarding the outcome mRS are presented in this paper, both the pre-defined main outcome mRS 6 months after inclusion and the mRS scorings after 3 months. The results have been analysed in several ways, including side-by-side comparisons of mRS scorings in the three groups, comparisons of change scores, comparisons of within-group changes, and comparison of the two intervention groups vs. the control group with mRS scorings dichotomised to dependence (mRS>2) or independence (mRS≤2). We found only modest differences between the three randomisation groups, and only in a few instances reaching statistical significance. However, the trend was quite clear with the intervention groups generally doing better than the control group. In addition there were no clear differences between the two intervention groups.

There are several possible reasons for the results demonstrating only a few statistically significant differences between the groups. One reason may obviously be that there is no difference in functional outcome between our two ESD schemes and ordinary treatment, but we find this explanation unlikely. Since the results showed a quite clear trend in one direction (the intervention groups scored better than the control group) we think that the non-optimal power of the study is a main cause for generally not reaching statistically significant results.

The basis for the power calculations were the results from the study conducted in Trondheim during the period 1995-1998 (26), which showed a very clear benefit of ESD compared to the ordinary treatment of that time. In retrospect, such a clear difference could probably not be expected today, due to the much improved stroke treatment now, including better rehabilitation and a generally far better secondary stroke prophylaxis. This would putatively lead to the obtainable benefits of improved rehabilitation being smaller, and therefore needing a higher number of patients to demonstrate the difference with statistical significance.

A third reason for the small outcome differences may also be the outcome measure – mRS – being too blunt to detect the intervention effects. Although the results

concerning this measure were inconsistent, the participants in the two intervention arms were generally very content with the close and personal rehabilitational follow-up inherent in this study. They also scored higher on patient satisfaction than the control group, especially at 3 months which was closest to the intervention period. In retrospect, the additional use of patient-reported outcome measures might have been more likely to demonstrate differences between ESD and control arms.

An additional observation from the results is the intervention effect being most pronounced at 3 months evaluation, but then clearly declining at re-evaluation 6 months after inclusion. We also observed better improvement in men than in women, which is in accordance with many previous reports. These points will be further discussed later in this thesis.

The Cochrane report states that ESD may be most beneficial for moderately affected stroke patients (3). We therefore explored the possibility that subpopulations of the patients might benefit selectively from the two ESD schemes by performing subgroup analyses. We found, however, no differences according to the degree of stroke severity expressed by NIHSS score. Analysed according to discharge destination the findings were generally also negative, but the patient trajectory stroke unit to DPMR to home, followed by structured community rehabilitation, showed significant difference between the study arms with least effect in the control group. This might indicate that severely affected stroke patients will benefit selectively from a combination of specialised in-patient rehabilitation followed by structured community rehabilitation.

A very interesting finding was the virtual identical length of stay in the stroke unit for the three randomisation arms (mean 11.4 days), despite specific efforts to discharge the patients in the ESD 1 and ESD 2 arms early. This finding strongly indicates that stroke patients today – at least in our university hospital – are discharged as soon as they are able to stay in their homes and that there is nothing more to gain in this respect. For the stroke patients included in our study two factors obviously were important for in-patient time in the stroke unit: how soon the patients could be safely

discharged to their homes (mean 8.3 days in the stroke unit for this group) and how long they had to wait for additional transfer to a specialised rehabilitation unit or another institution when that was needed (mean 15.4 days in the stroke unit for this group).

6.4 Paper 3

In Paper 3 the effects of the three treatment modalities were explored 3 months after the incident stroke in the subpopulation of participants in the ESD Bergen Stroke study who were discharged directly from the stroke unit to home. This subpopulation was chosen because of its homogeneity and comprised 167 of the 306 participants (55%). The primary outcome for this study was Postural Assessment Scale for Stroke (PASS), which assesses the patient's ability to maintain a position and to maintain equilibrium during various positional changes (40). There was no significant difference between the groups on this outcome.

Significant differences between the groups were, however, demonstrated regarding three of the secondary outcomes. These outcomes were the Trunk Impairment Scale-modified Norwegian version (TIS-modNV), which assesses trunk control, and self-reported problems with walking and ADL assessed on a numeric rating scale (46). For all these three least improvement was seen in the control group. However, pairwise comparisons failed to show a significant difference between any two groups for TIS-modNV, but did so for the two self-report problem areas. Self-reported problems with walking improved significantly more in the ESD 1 group and ADL problems improved significantly more in the ESD 2 groups, both compared to the controls.

These differential findings may tentatively be ascribed to the different treatment settings, which also led to somewhat differing treatment profiles. Day unit rehabilitation focused more on physical training and also encompassed transfer from the patient's home to the day unit three times a week, and both these circumstances

could be expected to improve subjective walking capacity as well as walking speed more than home treatment. The home rehabilitations group's activities, on the other hand, were more directed towards various domestic tasks and activities, and hence would be expected to improve ADL capacity more selectively.

There was a clear difference in the total amount of treatment between the ESD 1 and ESD 2 groups in this study. This difference was not intended, but possibly is a consequence of the multidisciplinary community health team's members' time schedule. One might speculate whether this difference contributed to the better improvement in walking ability in the ESD 1 group.

The patients studied in this paper were those who did not need an additional institutional stay before discharge to home. They generally were mild-to-moderately affected, and the findings reported in Paper 3 therefore cannot be generalised to more severely affected stroke patients. Also, the substantial loss to follow-up of 37% indicates caution in interpreting the study results.

Paper 3 focused on some of the main ESD Stroke Bergen study's secondary outcomes regarding physical activity, especially trunk control and walking, in addition to self-report on several aspects of function including ADL. The study population were those stroke patients which were discharged directly from the stroke unit to home. Occupational Therapist Tina Taule has also studied this specific subgroup of patients at 3 months and compared the effects of the three different treatment modalities on Assessment of Motor and Process Skills (AMPS), which is an outcome in the activity domain of the ICF (57). AMPS is used to explore the patient's ability to perform a self-chosen ADL task in a familiar environment and in the way he or she usually does it. After completion of each AMPS task observed by a certified occupational therapist the patient's quality of performance on each of several items is scored according to a manual (58).

Taule's cohort was all patients tested with AMPS both at baseline and 3 months, 103 patients in all. She reports highly significant improvement in AMPS from baseline to 3 months across all three study groups, but no significant differences between the

groups. However, regression analysis demonstrated a statistically significant association between randomisation group and mRS score as well as dichotomised mRS score (57). This finding is another indication that patients receiving ESD do somewhat better than controls.

6.5 Paper 4

All stroke patients participating in the ESD Stroke Bergen study were extensively evaluated at baseline and the data entered into the NORSTROKE data base (59). This standard procedure enabled us to systematically explore the possible predictive effect of registered variables on the main outcome mRS. Both predictors for the mRS score at 6 months (representing the absolute functional level of the patient at 6 months) and predictors for the change in mRS from stable baseline to 6 months (representing the functional improvement during that period) were searched for using multiple regression analyses. We also decided to do separate analyses on the full stroke population and the infarction subgroup, since cerebral infarction must be considered a pathogenetically more homogenous group than the total stroke group.

The results were quite different for the two different outcomes mRS at 6 months and mRS change from baseline to 6 months, with generally much fewer predictors for the latter. The main predictor for mRS at 6 months was BI at stable baseline. Since BI is an alternative scoring for the degree of independence or dependence based on ADL competence, and hence the predictor with the closest relationship to mRS, this finding was to be expected. It also parallels the main finding in many previous studies on stroke outcome predictors, where the severity of the incident stroke repeatedly has been shown to be a strong predictor of functional outcome (60-67).

Age and sex were by choice kept in all analyses. The effect of age was ambiguous, whereas female sex generally was a negative predictor for mRS at 6 months. Also previous cerebrovascular disease, peripheral artery disease, pneumonia or necessity for tube feeding in the acute phase, and leukoaraiosis turned out as negative

predictors for functional outcome in one or both analyses (total group or infarctions only). Thrombolysis performed was a positive predictor in the infarction group. These findings are consistent with previous reports, especially concerning the negative predictive effect of female sex and previous cerebrovascular disease (60;62;64;65). The acute phase conditions mentioned above most probably signify more seriously affected patients and therefore show as negative predictors.

Poorer functional outcome in women than in men has been described in several previous studies (62;66;68-76) and also in reviews (77;78), but no sex difference has also occasionally been reported (60;63). In our study a sex difference was also demonstrated in Paper 2 where men scored significantly better than women on mRS 3 and 6 months after inclusion.

For the mRS change from stable baseline to 6 months only a few variables were of predictive importance. Previous cerebrovascular disease, female sex and the necessity for tube feeding in the acute phase were negative predictors in one or both analyses.

The variable “subjective health complaints” as well as some others was introduced during the study, leading to a limited number of patients being scored (53%). These variables were therefore left out from the regression analyses leading to elaboration of final models, but instead added to these final models afterwards. Subjective health complaints were scored using the Subjective Health Complaints Inventory described by Eriksen et al. (48), where respondents rate their subjective discomfort relating to 29 different bodily or psychological symptoms on a 4-point Likert scale from 0 to 3. These symptoms are further divided into five different subscales: musculoskeletal pain, pseudoneurology, gastrointestinal problems, allergy, and flu. In our study the respondents were scored during the first period in the stroke unit, and they were specifically instructed to rate their symptoms as they were in the period preceding the stroke.

Pre-stroke subjective health complaints turned out to be a very significant predictor in all four settings; i.e. for both the outcomes mRS at 6 months and mRS change from baseline to 6 months, and in both the total stroke group as well as in the infarction

subgroup. Apart from BI in the stable acute phase strongly significantly predicting mRS at 6 months, subjective health complaints was the strongest predictor defined in the study. We also found that subjective health complaints were much more prevalent in women than in men, which is in accordance with previous reports (79;80). Including subjective health complaints in the final prediction models ameliorated the influence of patient sex in all of them, and this strongly indicates that an important reason for women having a poorer recovery than men may be their higher load of subjective health complaints.

The selection criterion for scoring only a part of the patients for subjective health complaints was solely their later recruitment into the study, and no systematic difference between patients with and without subjective health complaints scored should therefore be expected. Comparison of all other variables between these two groups demonstrated only one minor difference, confirming this, and thereby strongly indicating that the findings regarding subjective health complaints are generalizable to the whole study population.

These findings relating to subjective health complaints are important in several ways. First, a high burden of subjective health complaints is a risk factor that can be readily detected early on after a stroke, and, secondly, subjective health complaints may be modifiable during the rehabilitation course if addressed specifically. Health workers treating the patients should therefore be aware of these complaints and take them into consideration when rehabilitating the patients. It is also noteworthy that subjective health complaints is by far the strongest predictor for the degree of change in functional capacity of all variables examined in our study.

6.6 General discussion

Previous research have demonstrated clear benefits of early discharge to home of patients after acute stroke, coupled with qualified support through the process and rehabilitation being offered to the patients when home-dwelling. The important

studies were, however, conducted 10-20 years ago, and one may reasonably question whether the major changes and improvements in stroke care during the intervening period have modified the additional benefit of an Early Supported Discharge approach today.

The RCT study posed two main objectives. The first was to explore the effects on functional outcome of an improved stroke rehabilitation chain based on ESD principles and including discharge to home as early as possible, support by a multidisciplinary coordinating team, rehabilitative treatment by a multidisciplinary community health team, and out-patient hospital follow-ups. The second aim was to compare the effects of the rehabilitative treatment given in two distinct and rather different settings: either in a day unit or in the patients' own homes.

6.6.1 Can a beneficial effect of ESD compared to ordinary treatment still be demonstrated?

The participating stroke patients were extensively examined and scored during the study period, including repeated assessments of mRS as the main parameter of functional capacity. Although most results indicated best results in the intervention groups, we were mostly not able to demonstrate this difference between the groups with statistical significance. We interpret this primarily as an indicator of insufficient power of the study, in particular relating to a generally improved stroke care with smaller room for further improvement. The additional effect of ESD-based stroke rehabilitation therefore seems to be more modest today, but still present. Early Supported Discharge is therefore still worthwhile.

Very interestingly, a study was recently published from the UK, examining ESD vs. non-ESD discharge from stroke unit to the community in a quasi-experimental cohort study (81). The authors found statistically significant differences concerning length of hospital stay, satisfaction with services received, functional outcome evaluated by BI, and health scores of the patients' carers. In Sweden a study is presently being

conducted, evaluating the effect of ESD in today's era with in-patient times much shorter than in previous published studies on ESD (82). The primary outcome in that study is levels of anxiety and depression, but functional level and health economic analysis will also be reported, among other secondary outcomes.

An interesting observation from Paper 2 is the time frame of the results, with a rather clear difference between the groups at 3 months, but to a large extent not at 6 months. This signifies a definite wash-out effect of the intervention results as early as a few months after the intervention has ended. This observation also points to the very general problem in stroke (and other) rehabilitation of how to maintain patient treatment effects over time. In stroke rehabilitation this to a large extent will depend on the patient and his or her ability to maintain acquired strategies and behavioural changes like physical training and other functional activities over time. A more continuous follow-up from the healthcare will probably be necessary to achieve this. So called "frisklivssentraler" (municipal health centres providing general health information, health promotion and training opportunities), which are being established in municipal areas in Norway, may be an important contributing element (83).

The long term functional prognosis for patients having suffered a stroke is insufficiently studied. One recent study however reports the five year motor and functional outcome from the prospective cohort study CERISE (84). The authors describe gradual improvement up to about six months after a stroke, but then gradual worsening during the following observation period with a result at five years about equivalent to the results two months after the stroke. Our RCT has led to a follow-up study where available and consenting patients are re-evaluated 3-5 years after their incident stroke (Aaslund et al., in preparation). The outcomes in this study include both functional scores (mRS, BI, NIHSS and others), physical test scores and physical activity monitoring using the ActivPal device (85), and the results will provide quite detailed additional information on the long term outcome in this patient subgroup.

6.6.2 Day unit rehabilitation, home rehabilitation, or both?

The two different varieties of ESD offered within the RCT trial comprised rehabilitation in a day unit or in the patient's home. Thus, the individual stroke patient received his or her treatment in only one of these two settings, irrespective of personal preference. The study results showed only minor differences in outcome between the two modalities. The main outcome in Paper 2 (mRS) did not differ, nor the main outcome in Paper 3 (PASS), but self-reported problems with walking and ADL differed significantly in some respects. Walking problems improved significantly more in the day rehabilitation group and ADL function more in the home rehabilitation group, compared to the control group. These findings are well consistent with the somewhat differing profile of the two modalities. Day unit rehabilitation was more training-oriented and could be expected to improve physical function like walking ability, while home rehabilitation should be anticipated to improve ADL more specifically. There were, however, no significant differences in side-by-side comparisons of the two intervention arms.

The question whether centre-based or home-based rehabilitation after stroke leads to the best functional outcome was discussed in a systematic review by Hillier and Inglis-Jassiem in 2010 (86). Their analyses were based on 11 trials comprising 1711 home-dwelling stroke patients, with Barthel Index being the main outcome. Some superior benefit of home-based rehabilitation was found in seven trials, whereas no difference was reported in four. They concluded that community post-stroke rehabilitation should shift towards home-based services, and taking cost (probably lower) into consideration strengthened this argument. Very interestingly, they also recommended that patient preferences regarding treatment arena should be listened to if both could be offered simultaneously (86).

Whereas the differences in rehabilitation outcome were only marginal between the two modalities day unit and home rehabilitation in our study, these two modalities have a different profile and represent different challenges for the stroke patients. We experienced a higher patient drop-out rate for day rehabilitation compared to home,

obviously related to the required transfer three times per week and in some instances also hampered by economic cost. Some patients preferred the day unit rehabilitation, which also represented a social setting where they could discuss their post-stroke situation with peers as well as the professional team members.

Altogether, the most preferable model seems to be a dual mode allowing for both modalities and according to both patient preferences and the community health team members' professional judgement. In addition, at least one home visit by the team is regarded necessary for most patients to evaluate their home situation and function.

6.6.3 Diversity of rehabilitation trajectories

Rehabilitation of a stroke patient may include rehabilitation in a specialised hospital department, an in-patient rehabilitation centre or in a municipal rehabilitation ward, in addition to out-patient community rehabilitation either by a designated community rehabilitation team or as conventional community rehabilitation outside of a team setting. This allows for many rehabilitation trajectories, and a further challenge will be to select the most suitable rehabilitation pathway for the individual patient. This was summarised in the community health team's report where six different trajectories were described for the patients in our study. These trajectories in different ways included the stroke unit, the Department of Physical Medicine and Rehabilitation (DPMR), privately owned specialised rehabilitation centres, municipal institutions, treatment by the community health team, and the early discharge home (56).

In Paper 2 some aspects of the general challenge of defining optimal patient trajectories were explored in the subgroup analyses, but without providing clear answers. We noted, however, that the ESD 1 and 2 group patients requiring additional institutional stay before discharge from the stroke unit to home and being admitted to the DPMR improved significantly more than the control group patients. This indicates that there are optimal rehabilitation trajectories for subgroups of stroke

patients, but further studies are needed to clarify and delineate this more precisely. This observation never the less emphasises the need for individualisation of stroke rehabilitation according to patient characteristics and needs.

6.6.4 Unmet needs

Our ESD rehabilitation chain was heavily based on the work of the two multidisciplinary teams involved; the hospital-based coordinating team and the community-based health team. They both consisted of physiotherapist, occupational therapist and nurse, and other health professions had to be contacted when needed. In medical issues the patient's regular general practitioner was available. Speech therapist and social worker were available as part of the ordinary community health care if needed. Beside this neuropsychological assessment and the service from a visual rehabilitation therapist were sometimes needed, but not readily available from the community healthcare. These professions should also be an integrative part of an optimal rehabilitation chain for stroke patients.

Within the framework of the ESD Stroke Bergen study Taule et al. have conducted a qualitative study interviewing eight patients from the ESD 2 (home rehabilitation) group (87;88). Although the patients were mildly affected by their stroke they perceived their life as existentially changed regarding both health and self-perception. They expressed profound feelings of loss and uncertainty regarding the future, as well as concern related to body, activities and societal participation. In this situation the informants perceived the caretaker's communication qualities and ability to attend to individual physical and psychosocial needs as important. This study of Taule et al. pinpoints patient needs that are seldom recognised, but are important aspects of the patients' lives which should also be taken into consideration in stroke rehabilitation.

In addition, a more permanent long-time follow-up, securing preservation of health-promoting measures introduced during the rehabilitation period is needed as previously discussed.

6.6.5 Limitations of the study

Our randomised controlled trial has some definite limitations. The suboptimal power has been discussed previously and obviously reduced the possibility of obtaining statistically significant results and thereby more definite answers to the research questions. The actual study power was further reduced by the relatively high drop-out rate. However, substantial efforts were made to obtain main outcome scorings of the participants, who belonged to a patient group of high age and with frequent comorbidity. A prolongation of the inclusion period would therefore probably have been necessary to increase the power, but this was not realistically possible.

Another weakness is the insufficient information regarding treatment received by the patients outside the organised ESD setting. The need for such information was acknowledged during the preparation of the study, but self-report forms did not work well with this patient group.

A third point concerns the choice of outcome measures. Using other, well selected patient-reported outcome measures could possibly have demonstrated outcome differences between the arms of a more qualitative nature.

7. Conclusions

The present study was a randomised controlled trial investigating the outcomes of stroke rehabilitation in two different Early Supported Discharge (ESD) modalities and a control group receiving treatment as usual (protocol reported in Paper 1). The two main objectives were to compare the results of ESD with ordinary treatment and to look for differential effects of the two ESD modalities (Papers 2 and 3). In addition, we wanted to evaluate the effects of several potential predictors on functional outcome (Paper 4).

The results demonstrated slightly better rehabilitational outcome for the ESD schemes compared to the control group, especially 3 months after the incident stroke, but very much attenuated at 6 months. These quite modest effects after ESD in our study probably are the result of at least two different, but related factors. First, the generally improved stroke care during the last 15-20 years, including rehabilitation services, has to a considerable extent diminished the potential benefits of further improved services. Secondly, the statistical power of our study was not optimal since the pre-determined number of patients was not reached. In addition, the power calculation was based on a larger treatment effect than could be realistically anticipated. These factors working together most probably offer a plausible explanation for the small differences observed.

There were only very discrete differences in outcome between the two ESD groups, though the treatment profiles were somewhat different. Each of the two ESD modalities has benefits and weaknesses, and the individual stroke patient may be more suited for one or the other of the schemes. We therefore consider a more tailored approach to be optimal, with each patient being considered individually for the most beneficial combination of the two modalities according to both individual preference and professional judgement. This procedure has also been adopted as standard practice for the community health teams after the completion of the study.

The study has demonstrated the feasibility of establishing and maintaining an improved rehabilitation chain in our municipality, and this new rehabilitation

infrastructure has become a permanent service after the completion of the study. The concept has also gradually been broadened beyond the stroke patient group with the introduction of other patient groups (traumatic brain injury and multiple sclerosis) into this early supported rehabilitation service.

The third objective of the study was to search for variables predicting functional outcome, including absolute functional level expressed as modified Rankin Scale (mRS) at 6 months and functional improvement from stable baseline to 6 months expressed as change in mRS. This was explored by regression analyses. Baseline function expressed as Barthel Index was a very strong predictor for mRS at 6 months, which was to be expected and also has been demonstrated in many previous studies. Self-reported subjective health complaints pre-stroke also strongly predicted functional outcome in the subgroup of patients who were scored for this, in addition to being the only strong predictor for functional improvement from baseline to 6 months. There were only minor differences between the cohorts with and without subjective health complaints scored and the findings are therefore probably generalizable to the whole patient group.

Female sex was generally a fairly strong negative predictor both for function and functional improvement at 6 months when subjective health complaints were not included in the analyses, but introducing this variable removed the negative predictive effect of female sex. Subjective health complaints were much more common among women in our cohort and we think that the women's higher load of such complaints may be important for their generally poorer functional prognosis after stroke.

8. Implications of the study and future considerations

Early patient discharge from hospital to home after stroke diminishes the rehabilitation demands on the specialist health care while at the same time necessitating well-structured rehabilitation schemes within the community health care. This system change will be increasingly necessary in the future as a consequence of the ageing population, resulting in increased number of stroke patients and rehabilitation needs. Previous studies conducted 1-2 decades ago demonstrated that such early discharge also improved patient functional outcome and reduced the need for permanent institutional care. Our study conducted in recent years still shows equal or better outcome following early discharge, but no further reduction of days spent in hospital.

Based on these considerations a further build-up of structured community rehabilitation services must be strongly recommended as an integral part of community health care. The models may vary, but a coordinated discharge from hospital and services from a multidisciplinary health team must be regarded as cornerstones of post-stroke community rehabilitation. The members of this team must be skilled in the physical issues relating to stroke, but in addition have a sound understanding of psychosocial as well as existential consequences and how to meet and counteract these. Furthermore, based on the experiences from our study both the patients' homes and a day unit are suitable arenas for the community rehabilitation after stroke. A combination of arenas according to therapist and patient preference is recommended, and the duration of the intervention should be tailored to individual needs.

The recommendation of Early Supported Discharge can, however, not be generalised beyond cities and urban areas. One main un-answered question from the Cochrane review is whether ESD is feasible and effective in rural areas. This question is still open due to lack of studies and, probably, the obvious difficulties inherent in establishing an efficient multidisciplinary service in rural areas with long distances

and sparse population. A Norwegian study has however been published in 2004, reporting the results of a randomised trial comparing ESD and standard service for stroke patients living in rural municipalities (30). No difference in functional outcome was reported in this study.

A major challenge for further improvement of stroke rehabilitation will be to maintain beneficial behavioural changes like increased physical activity and a generally healthier life style, often adopted in the post-stroke period. A recent Norwegian study compared the long term results of an intensive exercise group and a regular exercise group after stroke, but found no difference (89). This was interpreted as a result of both groups being encouraged towards physical activity during the first year of the project. The question of how physical activity should be promoted was explored in a recent qualitative study from the UK (90). The authors describe a range of personal beliefs and attitudes that influence the motivation to exercise and could be addressed, such as psychological motivation to exercise, beliefs about stroke recovery and a desire for a non-medicalised approach. Some kind of long-time service and follow-up also seems to be necessary. The organisation of such services, including the development and utilisation of effective patient incentives remains to be determined.

The experiences and results from the ESD Stroke Bergen project are most probably relevant for patients with other diagnoses needing rehabilitation as well, thereby suggesting that the model used in our project may be extended to rehabilitation more generally. The recent extension in our local community to include also patients with traumatic brain injury and multiple sclerosis is therefore a logical further step.

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