THE STROKE-UNIT DISCHARGE GUIDELINE

A PROGNOSTIC FRAMEWORK FOR THE DISCHARGE DESTINATION FROM THE HOSPITAL STROKE-UNIT

RONALD MEIJER

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moeder en wijlen mijn vader

Contents

Chapter 1

Introduction

Discharge decision from the hospital stroke-unit

In the Netherlands each year over 30.000 people suffer from a stroke, and according to estimates for the coming decades this number will increase, because of the ageing effect of the populations in Western Europe. First year post-stroke mortality is about 33%. The prevalence of post-stroke survivors is over 100.000. The annual costs amount to € 1 billion due to (para-)medical, rehabilitative, and nursing therapies, nursing home residential care, loss of productive labour, aids for activities of daily life, ambulation and household activities, residential adaptations and adaptations at the job.

The multitude of disturbances in crucial functions within the sensorimotor, cognitive and communicative domains may cause serious threats for the patients to remain independent in self-care.

According to Guideline number 7 of the Stroke Guidelines 2000 of the Dutch Institute for Quality in Health Care CBO[1] every patient with a suspected stroke should be admitted to hospital for a fast diagnosis, so that in case of a cerebral infarction thrombolysis could be given to a selected group of patients within three hours after start of the symptoms. Furthermore, every stroke patient should be transferred to a specialised stroke-unit (guideline 16), and medical and rehabilitative care should be organised in the form of a transmural stroke service (guideline 15). A fast and well structured communication and consultation between the various institutions is mandatory. The use of a transmural patient record can be a suitable instrument for this communication, and in future electronic patient records (guideline 17) can fulfill a similar function. Apart from a medical diagnostic examination, a multidisciplinary rehabilitation team should make a rehabilitation diagnosis, including screening for potential sensorimotor, cognitive and communicative impairments and disabilities as soon as possible. Preventive actions should be performed with respect

to known potential complications, and rehabilitative treatment should start at once (guidelines 28,30,32).
Next, a quick and well-considered choice of the discharge destination is very important to realise the optimal rehabilitation route for the individual patient. In the Netherlands for the majority of patients this decision will be made around day seven to ten post stroke by a multidisciplinary treatment team. The lack of evidence based criteria to formulate the discharge destination from the stroke unit is a problem, and uncertainty often exists about the correctness of the decisions taken[2]. The CBO Stroke Guidelines 2000 do not contain a discharge guideline. The clinical knowledge of the members of the multidisciplinary treatment team is the basis for this decision. Previous research in the Academic Medical Centre Amsterdam showed that 14% of patients were discharged from the hospital to a non-optimal discharge destination[3]. The costs of a wrong discharge destination are huge: the unintentional use of hospital beds for services inherent to a nursing home, and at the level of the individual patient a wrong rehabilitation program that decreases the chances of a favourable outcome.

The choice of the discharge destination from a hospital stroke-unit is often based upon the prognosis for future ADL (activities of daily life) functioning and ambulation[4,5,6]. But ADL and ambulation alone do not account for independent living on one's own. Insufficient knowledge exists about which predictive factors determine the ability to live independently. Recovery after stroke is influenced by many factors, including psychosocial ones. Moreover, the presence of social support could be an important predictor of discharge destination[7,8]. In many cases the success of a return home is probably more affected by the characteristics of the primary caregiver, than by the characteristics of the stroke patients themselves.

Current problems concerning prognostic research in stroke

The problems concerning the scientific base of prediction in stroke are manifold. Numerous prognostic stroke studies do exist, but mutual comparison is impossible due to many reasons. For example, different outcome measures are used in effect studies, especially at the level of ADL and ambulation. The start of the inception cohort and baseline assessments in these studies begin at varying times post-stroke, whereas it is agreed upon that assessment within fourteen days post-stroke is mandatory for an early prediction at the hospital stroke-unit. Furthermore, the outcome assessments take place at different times post-stroke, whereas a minimal of six months post-stroke is recommended. There is variation in research populations such as restrictions to specific types of stroke (e.g. ischaemic stroke in medial cerebral artery domain), or age period. Few studies do exist that are based on future residence as outcome measure, which is remarkable because of the major importance of this item with respect to the choice of the discharge destination from the hospital. Only few studies could be found in which social factors have been assessed separately from clinical factors. From a clinical perspective we know how crucial the social domain can be to facilitate a return home. As will be outlined in this thesis, a systematic application of the recommendations of the "Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap"[9] is defective and as we shall show in our systematic reviews[10,11,12] few effect studies sufficiently meet criteria of methodological quality.

So, until now the prognostic studies seem to be weak, because of the absence of a conceptual model, which incorporates all prognostic factors including social ones and categorises them into sub-domains. Therefore,

post stroke validated patient profiles are missing during the subacute phase at the hospital stroke-unit.

Objective of the thesis and plan for developing the Stroke unit discharge guideline (SDG)

The objective of our research line is the development of a guideline, the Stroke-unit Discharge Guideline (SDG), which aims to realise an optimal discharge destination from the hospital stroke-unit. Our research plan for developing the SDG consists of the following steps (see table 1), of which the first four phases form the content of this thesis:

1. three systematic literature searches to prognostic clinical and social factors for future functioning in ADL and ambulation, future living situation, and discharge destination from the hospital stroke-unit

Table 1. Development plan Stroke unit Discharge Guideline (SDG)

This thesis	1.	Three systematic reviews to gather prognostic factors
	2.	Delphi procedure to determine total set of SDG factors
	3.	Delphi procedure to determine assessment instruments
	4.	Performance of multicentre prognostic cohort study in hospital stroke units. Data-analysis based on the first sample of 338 patients with respect to discharge destination as outcome variable
Continuing research	5.	Data-analysis of 1000 patients with respect to discharge destination and residence at one year post stroke as outcome variables
	6.	Construction of SDG algorithm

2. a Delphi procedure[13,14] to validate the results of the systematic reviews and to determine additional prognostic factors based on clinical experience, with participation of a multidisciplinary panel of clinical experts representing the key disciplines of the transmural stroke service chain nationwide
3. a definition of assessment instruments to measure the prognostic factors[15,16,17,18]
4. a prognostic cohort study with the discharge destination as outcome variable[19]

Construction of guidelines with use of systematic reviews in combination with clinical knowledge gathered by a modified Delphi technique

Guidelines are systematically developed statements to assist practitioner's and patient's decisions about appropriate health care for specific clinical circumstances[20,21]. It can be considered as a "professional state of the art" with respect to a certain subject, but it can also be used as a "transparency model" that provides maximum clarity with respect to decisions or actions. Because of this characteristic it can reduce unwanted inter-professional variation, is useful for professionals, students, policy purposes and health insurance companies, not to mention its use for the patient and his relatives.

Guidelines often rely on systematic reviews of literature that was published previously.

Systematic reviews can be of great help in guideline development because they involve the searching for, selecting, critically appraising, and summarizing results of primary research[22]. However, most of the time not all questions can be answered by systematic reviews. In an ideal

world, clinical guidelines would be based on evidence derived from rigorously conducted empirical studies. In practice, there are few areas of health care where sufficient research-based evidence exists or may ever exist[23]. In such situations, the development of guidelines will inevitably have to be based partly or largely on the opinions and experience of clinicians and others with knowledge of the subject at issue[24]. There are two main ways in which judgement-based guidelines could be devised: have the 'best person' make the judgement, or have a group do it. In theory, there are a number of advantages to a group decision, which will not be discussed here. But, if a group-based method is chosen, methods are needed for organising subjective judgements, given the diversity of opinions that may be expected in any group of people considering a topic. It is essential to be clear about what consensus development is and what it is not. It is a process for making policy decisions, not a scientific method for creating new knowledge. At its best, consensus development merely makes the best use of available information, be that scientific data or the collective wisdom of the participants.

There is a spectrum of methods for aggregating the judgements of individuals which can be characterised by the extent to which the method is implicit or explicit. Implicit methods tend to be qualitative or involve simple quantitative techniques (such as a majority vote). Explicit methods tend to be more complex, involving statistical methods in which judgements are combined according to mathematical rules, for example by taking the mean of individual judgements. Methods such as consensus development conferences rely on implicit methods whereas the Delphi method uses explicit, mathematical integration.

We used a 'modified Delphi' procedure, which is the most commonly used method for clinical guideline production. It is developed by the RAND Corporation during the 1970s and 1980s[25]. Initially individuals express their views privately via mailed questionnaires. The collated

results of the questionnaire are fed back to each member of the group when they are brought together to discuss their views, after which they again privately record their views on a questionnaire.

Evidence-Based Practice

Nowadays, evidence-based medicine has become an accepted basis for good clinical practice, and considerable efforts are made to implement it. In evidence-based health care, scientific information (evidence), preferably obtained from randomised controlled clinical trials, must be integrated with the clinical experience of the practitioner. This links clinical practice with research, and vice versa. Our final aim to construct the Stroke-unit Discharge Guideline (SDG) fits into this approach. As in the client centred approach, evidence-based practice aims at ameliorating individual patient care by not letting treatment options depend on the experience of the practitioner alone. Moreover, evidence-based practice propagates deviating from guidelines when the patient's situation demands this.

In our research we used the principles of evidence-based practice, which can be described as the conscientious, explicit and judicious use of current best available evidence in making decisions about the care of individual patients, integrating individual clinical expertise with the best available evidence from systematic scientific research[26]. The concise practice of evidence-based medicine comprises five steps[26]:

1. converting the need for information into an answerable question
2. tracking down the best evidence with which to answer that question
3. critically appraising the evidence for its validity, impact, and applicability
4. integrating the critical appraisal with clinical expertise and with the patient's unique biology, values, and circumstances

5. evaluating the effectiveness and efficiency in steps 1-4, and seeking ways to improve them both for the next time.

There is little dissent to the principles of evidence-based practice and the need for research into current practices has been acknowledged and embraced by many health care practitioners. Moreover, it is satisfying to read the results of a clinical trial which 'proves' the efficacy of a treatment approach that we are currently using in clinical practice. However, what of the evidence that is not supporting some particular practice? Have we been incorrect in using this method all these years? And if we have, what about the treatments that are based on these premises?
It must be appreciated that the randomized clinical trial is but one method of research, albeit an important one, that contributes to evidence-based practice. Longitudinal research methods investigating long term outcome of injury and disease also make a valuable contribution to the evidence base. Another area that is particularly important deals with prognostic studies directed towards identifying patient-profiles to match with certain interventions. In case of the SDG, this encompasses identifying patient-profiles with respect to rehabilitation needs and rehabilitation route.

However, some authors expressed concerns about evidence-based health care[27,28,29,30,31,32.] They argued that the move towards evidence-based medicine has come from the medical profession and, as a consequence, in practice this movement has tended to be focused on the doctor, rather than on the patient[27]. Evidence-based medicine could therefore lead to the setting of irrelevant or one-sided objectives in treatment[28] and irrelevant research questions[29], or weaken the role and importance of the patient's preferences and values[30]. Furthermore, especially in rehabilitative care, a patient's responsibilities with regard to carers or

her/his opinions with regard to quality of life may lead to preferences for treatment that are not primarily based on the best evidence from a biomedical point of view[31,32].

The concept of evidence-based medicine, however, remains important and necessary in clinical practice. To put it simply, there is no reasonable alternative for the thorough evaluation of the efficiency and effectiveness of treatments[33]. As yet, most evidence has been sought for the clinically relevant biomedical aspects and processes of disease. Appropriate rehabilitation outcome parameters like participation are more complex and often difficult to observe, which could hamper a rational evaluation of treatment options. The SDG can make a valuable contribution as a decision instrument for choosing an optimal discharge destination. However, one should realise that the rehabilitation process is multidimensional and multidisciplinary, acting on another complex system (the patient in a personally unique context)[34]. Therefore, it probably is not realistic to assume that in the near future definitive evidence will emerge for all aspects of rehabilitative care, but this too is in accordance with evidence-based practice: there must always be some space for treatment options that are perceived as supportive and helpful, if based on the clinical experience of the practitioner, the perception of the patient, or the best available evidence at that moment.

Useful clinical guidelines should contain more than clear recommendations. The evidence and reasoning on which the recommendations are based should be explicit, and the expected outcomes of implementing the guideline should be stated. Before completion of each guideline, the impacts on all pertinent outcomes (i.e., health status, patient satisfaction, provider satisfaction, cost and utilization, and capital needs) should be determined by developing a balance sheet[35,36].

Outline of the thesis

We performed our research in accordance with the Cochrane Collaboration criteria[37], we used adequate binary outcome strategies as advised by the Evidence-Based Medicine Working Group[38], and in the presentation of our systematic reviews we applied the methods suggested by Moher et al.[39], which contain a checklist of standards that describes the preferred way to present the Abstract, Introduction, Methods, Results and Discussion sections of a meta-analysis or a systematic review, and which provide a flow diagram providing information about the number of studies identified, included, and excluded and a taxonomy of the reasons for excluding studies.

In **Chapter 2**, we analysed the results of our first systematic review to identify evidence based prognostic factors in the subacute phase after stroke for activities of daily living and ambulation at six months to one year after stroke.
Our second systematic review **(Chapter 3)** deals with the identification of prognostic factors in the subacute phase after a stroke for the future residence at six months to one year post-stroke.
Because these two systematic reviews did not yield sufficient social prognostic factors, which is contradictory to our clinical experience, we performed a third systematic review (**Chapter 4)** to identify prognostic social factors in the subacute phase after stroke for the discharge destination from the hospital stroke-unit.

As scientific evidence, gathered from our systematic reviews, was insufficient we extended the identified prognostic factors with factors coming from expert opinions of a multidisciplinary team of clinical experts nationwide. This was performed by a modified Delphi procedure[40,41] **(Chapter 5)**. More specifically, we wanted to create a

conceptual framework of prognostic factors, which is based upon scientific evidence and clinical experience.
In the literature of our systematic reviews and in known standard works we have looked for assessment instruments which are being used most frequently in stroke care, and subsequently we have searched for information regarding their reliability and validity **(Chapter 6)**.

In **Chapter 7** we present the first results of a relatively large-scale multicentre prospective cohort study concerning the application of the stroke-unit discharge guideline as a prognostic tool for the optimal discharge destination from the hospital stroke-unit.

In the general discussion section **(Chapter 8)** we further discuss the problems concerning prognostic research in stroke. We specify the subject of the research and explain how it was performed in accordance with evidence based practice. Next we discuss the results of the research, in particular regarding the development of the SDG, the first results of the prospective hospital cohort study, and the expected future results. These include the final goals, potential profit, relevance and impact of the guideline SDG. We conclude with the dissemination and implementation of the SDG, and a description of new developments in stroke care worldwide.

A **Summary** in English and Dutch concludes this thesis.

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Chapter 2

Prognostic factors for ambulation and activities of daily living in the subacute phase after stroke
A systematic review of the literature

Clinical Rehabilitation 2003; 17:119-129.

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Abstract

Objective: To identify evidence based prognostic factors in the subacute phase after stroke for activities of daily living and ambulation at six months to one year after stroke.

Design: Systematic literature search designed in accordance with the Cochrane Collaboration criteria with the following data sources: 1. Medline, Embase, Cinahl, Current Contents, Cochrane Database of Systematic Reviews, Psyclit, and Sociological Abstracts. 2. Reference lists, personal archives, and consultation of experts. 3. Guidelines.

Methods: Inclusion criteria were: 1) cohort studies of patients with an ischemic or haemorrhagic stroke; 2) inception cohort with assessment of prognostic factors within the first two weeks after stroke; 3) outcome measures for ADL and ambulation; and 4) a follow-up of 6 months to 1 year. Internal, statistical and external validity of the studies were assessed using a checklist with 11 methodological criteria in accordance with the recommendations of the Cochrane Collaboration.

Results: From 1027 potentially relevant studies 26 studies involving a total of 7850 patients met the inclusion criteria. Incontinence for urine is the only prognostic factor identified in three studies with a level A (i.e. a good level of scientific evidence according to the methodological score). The following factors were found in one level A study: initial ADL disability and ambulation, high age, severe paresis or paralysis, impaired swallowing, ideomotor apraxia, ideational apraxia, and visuospatial construction problems; as well as factors relating to complications of an ischemic stroke, such as extraparenchymal bleeding, cerebral edema, and size of intraparenchymal hemorrhage.

Conclusions: The present evidence concerning possible predictors in the subacute stage of stroke has insufficient quality to make an evidence-based prediction of ADL and ambulation after stroke because only one

prognostic factor was demonstrated in at least two level A studies, our cutoff for sufficient scientific evidence.
Keywords: prognosis, activities of daily living, ambulation, stroke-unit, systematic review.

Introduction

Planning the discharge destination from a hospital stroke-unit is mainly based upon the prognosis for future (dis-)abilities and the future residence of the patient. Because of the multitude of symptoms in crucial functions within the sensorimotor, cognitive and communicative domains a stroke may cause serious threats for the patients to remain independent in self-care or to be able to live independently with or without support. The lack of evidence based criteria that can be used to formulate the discharge destination from the stroke unit is a problem, and uncertainty often exists about the correctness of the decisions taken[1]. Empirical knowledge of the members in the multidisciplinary treatment team is the basis for the decision.

Previous research in our centre showed that 14% of patients were discharged from the hospital to a non-optimal discharge destination[2]. An inappropriate discharge destination may cause unnecessary psychological suffering for the patient and the families, potentially serious errors in long-term management[3], and inefficient use of health care facilities. With the goal to realise an optimal discharge destination we started the development of a guideline, the Stroke-unit Discharge Guideline. The basis of this guideline will be formed by scientific knowledge from systematic reviews to prognostic factors for functional recovery, and for the future residence after stroke, supplemented by expert clinical knowledge, and taking into account the social circumstances of the patient[4, 5, 6], which are also important in determining whether the patient

can return home. The objective of this review is to identify evidence based prognostic factors in the subacute phase after stroke for activities of daily living and ambulation at six months to one year after stroke. We only found one former review, by Kwakkel et al.[7] in 1996, about prediction for functional recovery in the subacute stage after stroke. This review we used as a starting point, while we based our conclusions upon more rigorous criteria for scientific evidence, as we shall describe below. Apart from prediction of ambulation and activities of daily living, other important outcome measures do exist, e.g. mortality, length of hospital stay, and health related quality of life, but these are not the subject of this review.

Methods

In the presentation of this systematic review we applied the methods suggested by Moher et al.[8], which contain a checklist of standards that describes the preferred way to present the Abstract, Introduction, Methods, Results and Discussion sections of a meta-analysis or a systematic review, and which provide a flow diagram providing information about the number of studies identified, included, and excluded and a taxonomy of the reasons for excluding studies.
In accordance with the Cochrane Collaboration criteria[9], we searched up to March 2002 for all relevant cohort (historical as well as prospective) studies published in English, German, French, and Dutch. Keywords were cerebrovascular disorders, stroke, activities of daily living, self care, physical disabilities/disability evaluation, functional outcome/outcome assessment, prognosis/prediction, cohort studies/analysis, and follow-up. Information sources were Medline, Embase, Cinahl, Current Contents, Cochrane Database of Systematic Reviews, Psyclit, Sociological Abstracts, reference lists, personal archives, expert consultations,

Guidelines of the Netherlands Society for Neurology (1996)[10], and Guidelines Stroke 2000 of the Dutch Institute for Quality in Health Care CBO[11]. The full search strategies are available from the author.
Inclusion criteria: all studies including patients with an ischemic or haemorrhagic stroke with a clearly defined inception cohort and assessment of prognostic factors within the first two weeks after stroke, and a follow-up duration of at least six months and a maximum of twelve months, and with outcome measures for activities of daily living and ambulation, corresponding to codes 30-46 of the ICIDH (WHO pages 157-162)[12].
Exclusion criteria: case studies, case series, non-systematic review articles, all studies that included patients with a transient ischemic attack (TIA) in which a separate analysis for patients with stroke was not possible; subarachnoid hemorrhage; studies with only housekeeping activities or the level of psychological, social and communicative functioning (e.g.: social interactions, professional activities, shopping, performance of memory tasks) as outcome measures; studies with less than 50 patients. We defined a prognostic factor as clinically relevant if there was a difference between groups of at least 20%. Power computation with use of α=5% and β=20% shows that at least 50 patients per study are needed to detect a difference of 20% in a dichotomised scaled factor and in a univariate analysis.

Methodological criteria for validity assessment and data abstraction

All relevant publications were tested for internal, statistical, and external validity according to the 11 methodological criteria used by Kwakkel et al.[7] in their systematic review [Table 1].

Table 1. Binary outcome strategies rated "adequate" (Kwakkel et al.[7])

Outcome strategies	**Criteria**	**Criterion in Table 3**
To evaluate internal validity		
Measurements reliable and valid? Dependent variable	Positive, if the prognostic study tested the reliability and validity of measurements used or referred to other studies which had established reliability and validity	A
Measurements reliable and valid? Independent variable		B
Inception cohort during observation period?	Positive, if observation started within 2 weeks after stroke	C
Appropriate end-points for observation?	Positive, if observation ended a minimal of 6 months after stroke	D
Control for drop-outs?	Positive, if drop-outs durirg period of observation are specified	E
To evaluate statistical validity		
Statistical validation of relationship between dependent and independent variables?	Positive, if relationsbip between dependent and independent variable is tested for statistical significance	F
Sample size (n) adequate in relation to the number of determinants(K)?	Positive if ratio n: K exceeds 10 : 1	G
Control for multicollinearity?	Positive, if interaction between two or more independent variables is tested in the prediction model	H
To evaluate external validity		
Specification of relevant patient characteristics? (i.e. age, type, number, and localization of stroke)	Positive, if age, type, localization as well as number of strokes are specified in the cohort	I
Description of additional medical and paramedical interventions during observation?	Positive, if information on medical and paramedical treatment was reported	J
Cross-validation of the prediction model in a second independent group?	Positive, if the prediction model is validated in a second independent group of stroke patients	K

These criteria have been recommended by the "Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap"[13] in order to improve the scientific quality and comparability of stroke outcome research. The criteria are in agreement with the general recommendations for studying prognosis in this field[14, 15].

A binary weight (0/1) was given to each of the 11 methodological criteria listed in Table1. All prognostic studies were scored according to these criteria by two reviewers (RM,DI). Any disagreements were resolved by discussion or, if necessary, by consulting a third reviewer.

Using the criteria as shown in Table 2, we classified the publications included in this review according to level of scientific evidence, where A means good, B moderate, and C poor evidence. Like Kwakkel et al.[7] we gave a higher value to internal and statistical items. Only studies with level A were used for the best-evidence synthesis.

Table 2. Level of evidence

Level	Criteria
A	Studies that satisfy all items for internal and statistical validity (= 8 points or more)
B	Studies with a total score > 6, but not fulfilling criteria for level A
C	Studies with a total score ≤ 6

Results

From the initially identified 1027 studies, we selected 135 publications on the basis of the title and the abstract. In case of uncertainty regarding the inclusion, the entire text of an article was read. Twenty-six articles, involving a total of 7850 patients, fulfilled all our search criteria for the systematic review. The number of patients included in the studies ranged from 57 to 1197. These articles were then evaluated according to the 11 mehodological criteria in Table 1.

The results of the methodological scoring are summarized in Table 3.

Table 3. Methodological assessment

				Internal validity					Statistical val.			External val.			Score	Level
1st author	**year**	**Ref**	**N**	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	max 11	
Barer	1989	3	277	1	0	1	1	1	1	1	1	0	1	1	9	B
Barer	1990	16	362	1	0	1	1	1	1	1	1	0	1	0	8	B
Elmståhl	1996	17	66	1	0	1	1	0	1	0	0	1	0	0	5	C
Geerts	1995	6	63	1	1	1	1	1	1	0	0	1	1	0	8	B
Gompertz	1994	18	361	1	0	1	1	1	1	1	1	0	0	1	8	B
Heiss	1994	19	76	1	0	1	1	1	1	1	1	1	1	0	9	B
Hénon	1999	20	202	1	1	1	1	1	1	0	0	1	0	0	7	B
Jehkonen	2000	21	57	1	1	1	1	1	1	0	1	1	1	0	9	B
Jørgensen	1995	22	626	1	1	1	1	1	1	1	0	1	1	0	9	B
Jørgensen	2000	23	1197	1	1	1	1	0	0	1	0	1	1	0	7	B
Juvela	1995	24	156	1	0	1	1	1	1	0	0	1	0	0	6	C
Lampl	1995	25	279	1	1	1	1	1	1	1	0	1	0	0	8	B
Lin	1996	26	150	1	1	1	1	0	1	0	0	1	0	0	6	C
Lincoln	1997	27	315	0	0	1	1	0	1	1	1	1	0	0	6	C
Motto	1998	28	554	1	1	1	1	1	1	1	1	0	0	0	8	A
Mukherjee	1997	29	80	1	0	1	1	1	0	0	0	0	0	0	4	C
Pedersen[a]	1996	30	524	1	1	1	1	0	1	1	1	1	1	0	9	B
Pedersen[b]	1996	31	650	1	1	1	1	0	1	1	1	1	1	0	9	B
Samuelsson	1996	32	81	1	1	1	1	1	1	0	0	1	1	0	8	B
Sánchez-Blanco	1999	33	92	1	0	1	1	1	1	0	1	1	1	0	8	B
Stone	1993	34	171	1	0	1	1	1	1	1	1	1	0	0	8	B
Sveen	1996	35	74	1	1	1	1	1	1	1	1	1	0	0	9	A
Taub	1994	36	225	1	1	1	1	1	1	1	1	0	0	0	8	A
Thommessen	1999	37	171	1	1	1	1	1	1	1	1	0	0	0	8	A
Wade	1987	38	976	1	1	1	1	1	1	1	1	0	0	0	8	A
Wyller	1997	39	65	1	1	1	1	1	1	1	1	1	0	0	9	A

Year: year of publication; Ref: reference number in the text; N: number of patients recruited in the study; A to K: criteria for methodological score as described in Table 1; Score: total score of A to K; Level: level of evidence as described in Table 2.

Table 4. Results of level A articles.

First author	Purpose of the study and Population	Prognostic factors
Motto	To evaluate the prognostic value after ischemic stroke of complications such as development of parenchymal hemorrhages, extraparenchymal bleeding, and cerebral edema in 554 patients	Presence on CT scan of 1) intraparenchymal hemorrhages, 2) extraparenchymal bleeding and 3) cerebral edema, alone or in association
Sveen	Evaluation of the ASB in an inception cohort of 74 patients admitted to hospital	The six subscales of the ASB
Taub	To predict functional outcome at 1 year in 639 first-time strokes of a population-based cohort, younger than 75 years in a geographic area	Initial coma , paralysis, speech or swallowing problem , urininary incontinence, age, sex, district of residence, ethnic origin, and living alone before the stroke
Thommessen	To identify predictors of outcome after 12 months in 171 stroke patients admitted to a geriatric ward for rehabilitation from the acute unit after a mean length of stay of 9 days	BI, SMES, MMSE, urinary incontinence as in BI
Wade	Early prediction of outcome in a 976 population based cohort study	BI, urine incontinence, arm, leg and total Motricity scores, visual fields, cognitive function, sitting balance, IQ, loss of consciousness at onset, age
Wyller	To study gender differences in functional outcome during a half year period in 65 stroke patients admitted to hospital within 14 days after the stroke	Gender was the only investigated prognostic factor

ASB[40]: Assessment of Stroke and other Brain Damage for assessment of cognitive functions, which includes speech quality, language, auditory comprehension, ideomotor apraxia, ideational apraxia, visuospatial constructive subtest
BI: Barthel ADL Index, which measures activities of daily living and ambulation
SMES[41]: Sødring Motor Evaluation of Stroke Patients with subscores for arm, leg and gross motor function
MMSE: Mini Mental Status Eximination for cognitive impairment, which includes orientation, memory, attention and language

Outcome factors	Main results
Death, 5-item modified Rankin Scale by telephone interview 6 months post- stroke	The complications extraparenchymal bleeding and cerebral edema are independent prognostic findings for an unfavorable outcome (death or survival with a Rankin Scale Score of ≥ 3). Unfavorable outcome correlated with size of intraparenchymal hemorrhage
Survival. BI, FAI, IADL one year after stroke	None of the prognostic factors predicted survival. Ideomotor apraxia predicted IADL. Ideational apraxia and the visuospatial-constructive variable both predicted BI, FAI and IADL
BI 12 months after stroke	Initial paralysis, incontinence, and swallowing problems are predictors for bad functional recovery. No influence found for initial coma, speech problems, and demographic characteristics
Survival. Social functioning (FAI) 1 year after stroke	Urinary incontinence and male gender are independent predictors for survival during the first year. Higher BI sumscore is the only independent predictor for higher FAI sumscore
BI 6 months after stroke	Higher initial Barthel score within 7 days after stroke, lower age, "worse" sitting balance/trunk control, no/less urine incontinence predicted a better functional level
1 year after stroke: SMES with subsocres for arm, leg and gross motor function. ASB as cognitive test. BI for evaluation of primary ADL function	Men performed significantly better than women for the total BI, mobility, stairs and bathing as single items of the BI, the trunk, balance and gait section of the SMES and the ideomotor apraxia section of the ASB

FAI: Frenchay Activities Index, which measures domestic chores, leisure and work, and outdoor activities
IADL: Instrumental ADL items (ability to use the telephone, to handle finances, and to administer own medication)

According to the criteria given in Table 2, the following classifications for the level of scientific evidence were found: six level A, 15 level B, and five level C.

Five studies investigated specific conditons: hemorrhage after acute ischemic stroke[28], intracerebral hemorrhage[24], supratentorial hemorrhage[25], stroke severity in atrial fibrillation[26] and lacunar infarction[32]. Only two studies[3,18] crossvalidated their results in an independent second study (item K). Only a third of the studies described paramedical and medical interventions (item J). Of the 26 studies, 19 studies used level of functioning as the only outcome measure, four studies used level of functioning and final residence as outcome measures[3,35,37,39], and three studies used level of functioning and discharge destination as outcome measures[22,30,31]. Most frequently used outcome variables were activities of daily living (18 studies), death (8 studies), residence (7 studies), social functioning (5 studies), ambulation (4 studies), and cognitive functioning (2 studies). Most frequently used assessment instruments were Barthel Index (17 studies), Mini Mental State Examination and Frenchay Activities Index (5 studies), Rankin Scale and Glasgow Coma Scale (each 4 studies).

The results from the six studies of level A are summarised in Table 4. In Table 5 the prognostic factors in all 26 studies have been ranked according to level of scientific evidence for the studies.

Table 5. Ranking of prognostic factors according to level of scientific evidence for the studies (numbers correspond with the references)

Prognostic factors	**Level A**	**Level B**	**Level C**
Incontinence for urine	36,37, 38	16	29
Initial disability in ADL and ambulation	38	3,22,23,30 33	
High age	38	16,19,21,30 33,34	24,29
Severe paresis or paralysis		16,23,33,34	29
Swallowing problems	36	16	
Complications of an ischemic stroke: extraparenchymal bleeding, cerebral edema, size of intraparenchymal haemorrhage	28		
Ideomotor apraxia, ideational apraxia, visuospatial contruction problems	35		
Disorientation in time and space		16,23,30	
In supratentorial hemorrhages: Glasgow Coma Scale score, size of the hematoma, intraventricular blood expansion and localization		25	24,29
Comorbidity		30	
Unconsciousness/lowering of consciousness during the first 48 hours after stroke		16,18,23,26 33	24,29
Tactile/visual inattention, hemianopia		16,18,21,33 34	
Impaired mental status		3,33	
Conjugate gaze paralysis		16,23	29
Lower cerebral metabolic rate of glucose in noninfarcted brain regions in combination with hypertension		19	
Acute confusional state		20	
Poor sitting balance		33	
White matter hyperintensities on MRI in lacunar infarction		32	
Perceptional impairment using the Rey figure copy			27
Atrial fibrillation in ischemic stroke			26
Passive coping strategy and introvert personality			17

Discussion

Owing to the strict inclusion criteria the prognostic factors from this review are only valid for application within the first two weeks post-stroke, and for prediction of ambulation and ADL at six months to one year. Factors with high predictive quality in the first two weeks post-stroke could have different predictive quality in a later period, e.g. during the treatment in a rehabilitation center. Many articles were excluded because follow-up was too short, often three months or less, because patient selection was unclear and unexplained without a clearly defined inception cohort, and because assessment of prognostic factors took place after the first two weeks post-stroke. Since substantial recovery is possible[23,42] from three to six months after stroke at least six months follow-up has been recommended[3,43]. Unclear and unexplained patient selection presumably resulting in heterogeneous populations led to exclusion of many articles, because if the selection criteria have not been unambiguously specified, a valid basis for generalization of prognostic results is lacking. Pooling the results of this review in a meta-analysis was not possible, because no raw data were available. Furthermore heterogeneity across studies was huge. From the studies that investigated specific conditions[24,25,26,28,32] , such as stroke severity in atrial fibrillation[26], only the study of Motto[28] was a level A study and it yielded extra prognostic factors, different from the factors of the other level A studies from this review.

As level A prognostic factors, similar to those identified by Kwakkel et al., we found disability on admission, incontinence for urine, severe paresis and high age; but in our review the predictive value of unconsciousness, disorientation, poor sitting balance, and former stroke was not supported by level A studies. However, as level A prognostic

factors we also identified swallowing problems, ideomotor apraxia, ideational apraxia, visuospatial contsruction problems, and as complications of an ischemic stroke extraparenchymal bleeding, cerebral edema, and size of intraparenchymal hemorrhage, which factors were not identified in their review. More than moderate evidence existed for factors that have been supported by five level B studies, viz unconsciousness/lowering of consciousness during the first 48 hours after stroke, tactile/visual inattention, and hemianopia (see Table 5). The prognostic factor gender was not mentioned in Table 5, because the results of the studies were contradictory. In the study of Wyller et al. men performed better than women, in the study of Thommessen et al. men had a higher mortality, and the studies of Pedersen a and Pedersen b showed no gender differences in functional outcome.

The differences between the results of Kwakkel et al. and our results can be explained by the fact that they based their conclusions upon eight studies, which met all internal and statistical criteria, except item B about validity and reliability of used measurements, while our level A studies met all internal and statistical criteria, including item B. Furthermore, unlike their review, we excluded studies with less than 50 patients, we used more keywords in the search and our search included more digital databases and guidelines (see under methods section of this review); they only used Medline, Excerpta Medica and Current Contents. Our review included studies till 2002, while their review included studies till 1995. Two[36,38] of our level A studies were also selected by Kwakkel et al.[7], while our other four[28,35,37,39] level A studies come from the period after 1994.

Even articles of level A with a high methodological score showed methodological flaws. For example in the study of Motto et al.[28] there is insufficient insight into patient characteristics, because external validity

items (I, J and K) have not sufficiently been explained by the authors. In the study of Sveen et al.[35] quality and quantity of paramedical and medical interventions (item J) were not reported in the study, but they could have influenced results. Taub et al.[36] did not assess external validity (items I, J, and K), resulting in no insight into the proportion of patients who stayed at home or went to hospital, nor into the kind of rehabilitation treatment the patients received. Only 39% of patients had an initial CT scan, and types and extent of the stroke were not assessed. No difference has been made between severe or slight speech impairment as well as swallowing problems and between severe and slight/no paresis, which may have influenced the prediction for functional outcome. In the study of Thommessen et al.[37] there is insufficient insight into patient characteristics, because external validity (items I, J and K) has not sufficiently been assessed. The criteria for admittance to the geriatric ward were not specified. In the study of Wade and Hewer[38] the diagnosis of stroke had been made on a clinical basis and not by a CT-scan. Contrary to the experiences in clinical practice and known scientific literature,[44] in this study a poor sitting balance predicted good recovery. Wade suggested that this could inadvertently have been caused by multiple regression analysis. Because there was no insight into type or localization of the strokes in this study, the items I, J and K of external validity did not meet the criteria. Reported results are not valid for patients who were fully recovered within seven days after stroke, since these patients have been excluded from statistical analysis. Wyller et al. made no adjustment in the analysis for the difference in occupational background between the males and females; more males had a high-level education, which could introduce bias. If female stroke patients, who were older and more of whom were already permanently institutionalized, had received a higher threshold for referral to hospital,

this might explain the results of the study. Because a post-hoc hypothesis on unexpectedly found gender differences had been investigated, also chance could have contributed to the results, as well as quality and quantity of paramedical and medical interventions (item J), which were not reported in this study.

As shown in Table 5 incontinence for urine is the only prognostic factor that was found in more than one level A study. If one assumes that at least two level A studies are required to provide scientific evidence for a prognostic factor, this systematic review has only revealed one prognostic factor to determine ADL and ambulation: urinary incontinence. Moreover, if we critically review the articles, in which incontinence for urine was investigated, often insufficient information has been reported about crucial aspects. For example, was there premorbid existence of incontinence, was there stress incontinence or urge incontinence, how serious was the incontinence, and at what time after stroke was the incontinence assessed. Because the possible causes for the incontinence are manyfold (loss of decorum, bahavioral problems, disorientation in space with inability to find the toilet, paralysis with impossibility to handle a urinal, aphasia and inability to ask for help, urinary infections, severe illness, or a lesion in the bladder control centers in the cortex or brainstem), urinary incontinence is a complex clinical phenomenon. Therefore although in three level A studies incontinence for urine has been demonstrated to be a prognostic factor for the future functioning in ADL and ambulation, the underlying mechanism remains unclear.

Conclusions

The best evidence synthesis of level A studies results in the following prognostic factors for ambulation and ADL: incontinence for urine (the

only factor with good scientific evidence, demonstrated by three level A studies), low initial Barthel Index, high age, severe paresis or paralysis, swallowing problems, ideomotor apraxia, ideational apraxia and visuospatial-construction problems; and as complications of an ischemic stroke: extraparenchymal bleeding, cerebral edema, and the size of intraparenchymal hemorrhage.

What is lacking in the prognostic stroke studies till now are clear definitions of prognostic and outcome factors, guidelines for using assessment scales (which scale for which situation, and when to apply it), studies with a start of the assessment within two weeks post-stroke, and application of all the criteria that have been recommended by the "Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap"[13].

At this moment there are serious doubts about the scientific base for prediction in stroke.

IMPLICATIONS FOR CLINICAL PRACTICE

The prognostic factors we identified belong to the domains of biology (e.g. age), disease (e.g. localisation of the lesion), functions (e.g. paresis) and activities (e.g. Barthel Index). Based on these results we should advise, that prediction models for the discharge destination from the hospital stroke-unit should contain factors from all these domains. In our opinion the prognostic factors selected from level A studies should be used in clinical practice until further research provides new insights.

IMPLICATIONS FOR FURTHER RESEARCH

In many studies assessment instruments, such as the SSS or the MMSE, were used that comprise more than one domain. For future studies we would advise separate instruments to assess the prognostic qualities of each domain in order to make prediction possible. Also mandatory for

future research is a uniform and unambiguous definition of prognostic factors, such as urinary incontinence.
Another important finding of this review is that in the subacute phase after stroke relatively little research has been performed to predict the future level of functioning. Many prognostic studies have been done in the rehabilitation phase more than two weeks after stroke.
Generalizability of these studies is often limited, because selection of the study population is unclear. Long-term studies are needed to obtain more reliable data on differences in prognostic factors in the subacte phase after stroke and the rehabilitation phase.
For prediction of the discharge destination from the hospital stroke-unit research into prognostic factors at the level of activities of daily living and ambulation, as well as research concerning prognostic factors for the future residence and the importance of the social situation should be performed.

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Clinical Messages

- at the hospital stroke unit scientific evidence for prediction of ADL and ambulation is insufficient
- in the subacute phase post stroke relatively little prognostic research has been performed in contrast to the rehabilitation phase
- for future research, a uniform and unambiguous definition of prognostic factors is mandatory

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Chapter 3

Prognostic factors in the subacute phase after stroke for the future residence after one year A systematic review of the literature

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Abstract

Objective: To identify evidence-based prognostic factors in the subacute phase after a stroke for the residence at six months to one year post-stroke.

Design: Systematic literature search designed in accordance with the Cochrane Collaboration criteria with the following data sources: 1. Medline, Embase, Cinahl, Current Contents, Cochrane Database of Systematic Reviews, Psyclit, and Sociological Abstracts. 2. Reference lists, personal archives, and consultation of experts in the field. 3. Guidelines.

Methods: Inclusion criteria were: 1) cohort studies of patients with an ischemic or haemorrhagic stroke; 2) inception cohort with assessment of prognostic factors within the first two weeks after stroke; 3) outcome measures for future residence; and 4) a follow-up of six months to one year. Internal, statistical and external validity of the studies were assessed using a checklist with 11 methodological criteria in accordance with the recommendations of the Cochrane Collaboration.

Results: From 1027 potentially relevant studies 10 studies involving a total of 3564 patients, met the inclusion criteria. No prognostic factor was identified in at least two level A (i.e. a good level of scientific evidence according to the methodological score) studies, our standard for scientific proof. The following factors were found in at least one level A study: low initial ADL functioning, high age, cognitive disturbance, paresis of arm and leg, not alert as initial level of consciousness, old hemiplegia, homonymous hemianopia, visual extinction, constructional apraxia, no transfer to the stroke unit, non-lacunar stroke type, visuospatial construction problems, urinary incontinence, and female gender.

Conclusions: At present there is insufficient evidence concerning possible predictors in the subacute stage of stroke to make an evidence-based prediction of the future residence.
In the scientific research until now social factors and their contribution to the possibility of living independently have not been investigated, or at least less well . None of the studies in this review described a conceptual framework as basis for the choice of the examined prognostic factors.
Keywords: prognosis, future residence, stroke-unit, systematic review.

Introduction:

In a stroke-unit a fast and well-considered choice of the discharge destination is very important to realise the optimal rehabilitation route for the individual patient.
Most studies and decision models concerning the decision of the discharge destination from a hospital stroke-unit base their conclusions upon the prognosis for future ADL (activities of daily living) functioning and ambulation[1,2,3]. But the hypothesis that "the prognosis for future ADL functioning and ambulation is the same as the prognosis for the future residence" has not been investigated. Insufficient knowledge exists about which predictive factors determine the ability to live independently. This is the reason for the current literature search for studies which explicitly investigated the prognosis for the future residence in a period of six months to one year after the stroke.

Methods:

In the presentation of this systematic review we applied the methods suggested by Moher et al.[4], which contain a checklist of standards that describes the preferred way to present the Abstract, Introduction, Methods, Results and Discussion sections of a meta-analysis or a

systematic review, and which provide a flow diagram providing information about the number of studies identified, included, and excluded and a taxonomy of the reasons for excluding studies.
In accordance with the Cochrane Collaboration criteria[5], we searched up to March 2002 for all cohort (historical as well as prospective) studies published in English, German, French, and Dutch. Keywords were cerebrovascular disorders, stroke, activities of daily living, self care, physical disabilities/disability evaluation, functional outcome/outcome assessment, prognosis, cohort studies/analysis, follow-up, patient/hospital discharge, and housing. Information sources were Medline, Embase, Cinahl, Current Contents, Cochrane Database of Systematic Reviews, Psyclit, Sociological Abstracts, reference lists, personal archives, expert consultations, Guidelines of the Netherlands Society for Neurology (1996)[6], and Guidelines Stroke 2000 of the Dutch Institute for Quality in Health Care CBO[7]. The full search strategies are available from the author.
Inclusion criteria: all studies including patients with an ischemic or haemorrhagic stroke with a clearly defined inception cohort and assessment of prognostic factors within the first two weeks after stroke, and a follow-up duration of at least six months and a maximum of twelve months, and with future residence as outcome measure. Exclusion criteria: case studies, case series, non-systematic review articles, all studies that included patients with a transient ischemic attack (TIA) in which a separate analysis for patients with stroke is not possible; subarachnoid hemorrhage; studies with less than 50 patients. We defined a prognostic factor as clinically relevant if there was a difference between groups of at least 20%. Power computation with use of α=5% and β=20% shows that at least 50 patients per study are needed to detect a difference of 20% in a dichotomised scaled factor and in a univariate analysis.

METHODOLOGICAL CRITERIA FOR VALIDITY ASSESSMENT AND DATA ABSTRACTION

All relevant publications were tested for internal, statistical, and external validity according to the 11 methodological criteria used by Kwakkel et al. in their systematic review [Table 1][8].

PROCEDURE

These criteria have been recommended by the "Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap"[9] in order to improve the scientific quality and comparability of stroke outcome research. The criteria are in agreement with the general recommendations for studying prognosis in this field[10, 11]

A binary weight (0/1) was given to each of the 11 methodological criteria listed in Table 1. All prognostic studies were scored according to these criteria by two reviewers (RM and DI). Any disagreements were resolved by discussion or, if necessary, by consulting a third reviewer. Finally we classified the publications included in this review according to level of scientific evidence, where A means good, B moderate, and C poor evidence (see Table 2). Studies that satisfy all items for internal and statistical validity (≥ 8 points) received level A, studies with a total score > 6, but not fulfilling the criteria for level A received level B, and studies with a total score ≤ 6 received level C. Like Kwakkel et al. we gave a higher value to internal and statistical items.

Results:

From the initially identified 1027 studies, we selected 135 publications on the basis of the title and the abstract. In case of uncertainty regarding the inclusion, the entire text of an article was read. Ten articles involving a total of 3564 patients, fulfilled all our search criteria for the systematic review. The number of patients included in the studies ranged from 57 to 1197. These articles were then evaluated according to the 11 methodolo-

gical criteria in Table 1. The results of the methodological scoring are summarised in Table 2.

Table 1. Binary outcome strategies rated "adequate" (Kwakkel et al.)

Outcome strategies	**Criteria**	**Criterion in table 2**
To evaluate internal validity		
Measurements reliable and valid? Dependent variable	Positive, if the prognostic study tested the reliability and validity of measurements used or referred to other studies which had established reliability and validity	A
Measurements reliable and valid? Independent variable		B
Inception cohort during observatiion period	Positive, if observation started within 2 weeks after stroke	C
Appropriate end-points for observation?	Positive, if observation ended a minimal of 6 months after stroke	D
Control for drop-outs?	Positive, if drop-outs durirg period of observation are specified	E
To evaluate statistical validity		
Statistical validation of relationship between dependent and independent variables?	Positive, if relationship between dependent and independent variable is tested for statistical significance	F
Sample size (n) adequate in relation to the number of determinants(K)?	Positive, if ratio n : K exceeds 10 : 1	G
Control for multicollinearity?	Positive, if relationship between two or more independent variables is tested in the prediction model	H
To evaluate external validity		
Specification of relevant patient characteristics? (i.e. age, type, number and localization of stroke)	Positive, if age, type, localization as well as number of strokes are specified in the cohort	I
Description of additional medical and paramedical interventions during observation?	Positive, if information on medical and paramedical treatment was reported	J
Cross-validation of the prediction model in a second independent group?	Positive, if the prediction model is validated in a second independent group of stroke patients	K

Table 2. Methodological assessment

				Internal validity					Statistical val.			External val.			Score	Level
1st author	**year**	**Ref**	**n**	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**max 11**	
Friedman	1995	12	137	1	1	1	1	1	1	1	1	1	0	0	9	A
Geerts	1995	13	63	1	1	1	1	1	1	0	0	1	1	0	8	B
Jehkonen	2001	14	57	1	1	1	1	1	1	0	1	1	0	0	8	B
Jørgensen	1995	1	626	1	1	1	1	1	1	1	0	1	1	0	9	B
Jørgensen	2000	15	1197	1	1	1	1	0	0	1	0	1	1	0	7	B
Pedersena	1996	2	524	1	1	1	1	0	1	1	1	1	1	0	9	B
Pedersenb	1996	3	650	1	1	1	1	0	1	1	1	1	1	0	9	B
Sveen	1996	16	74	1	1	1	1	1	1	1	1	1	0	0	9	A
Thommessen	1999	17	171	1	1	1	1	1	1	1	1	0	0	0	8	A
Wyller	1997	18	65	1	1	1	1	1	1	1	1	1	0	0	9	A

Year: year of publication; Ref: reference number in the text; N: number of patients recruited in the study; A to K: criteria for methodological score as described in Table 1; Score: total score of A to K; Level: level of scientific evidence (see text).

As shown in Table 2, the following classifications for the level of scientific evidence were found: four level A, and six level B. Except the study of Thommessen et al. all studies sufficiently described relevant patient characteristics (item I). No studies crossvalidated their results in an independent second study (item K). Used assessment instruments were Barthel Index (8 studies), Frenchay Activities Index (4 studies), Scandinavian Neurological Stroke Scale (4 studies), Mini Mental State Examination (3 studies), Sødring Motor Evaluation of Stroke Patients and Assessment of Cerebral Stroke and other Brain Damage (2 studies), Scale of the Medical Research Council, Canadian Neurological Scale, Modified Motor Assessment Scale, Behavioural Inattention Test, Wechsler Memory Scale, and National Institute of Health Stroke Scale (1 study each). The results from the level A studies are summarised in

Table 3. Results of level A articles.

First author	Purpose of the study and Population	Prognostic factors (assessed < 2 weeks)	Outcome factors (assessed after 6-12 months)	Main results
Friedman	To examine predictors of returning home to live alone in a cohort of 178 elderly people who lived alone prior to stroke	Age, sex, pre-stroke BI, prior stroke, initial level of consciousness, arm and leg power, new hemiplegia, homonymous hemianopia, visual extinction, constructional apraxia, MMSE, transfer to the stroke unit, stroke type (lacunar or non-lacunar), and BI at day seven	Discharge residence (home alone versus not home alone). Follow-up residence at 2, 6 and 12 months (died, lost to follow-up, acute hospital, home alone, home not alone, institution)	All the investigated prognostic factors were significant for prediction of the residence at discharge and at the follow-up times except for age, gender, pre-stroke BI and prior stroke. The most powerful predictors were MMSE, homonymous hemianopia, BI score at day seven and leg power score
Sveen	Evaluation of the ASB in an inception cohort of 74 patients admitted to hospital	The six subscales of the ASB at 10 days from stroke onset	Place of residence (at home versus nursing home or death) 1 year post-stroke	The visuospatial constructive variable predicted return home. The praxic and language variables had no relationship to place of residence 1 year post-stroke
Thommessen	To identify predictors of outcome after 1 year in 171 stroke patients admitted to a geriatric ward for rehabilitation from the acute unit after a mean length of stay of 9 days	BI, SMES, MMSE, urinary incontinence as in BI, all assessed at a mean of 10 days from stroke onset	Place of residence (home versus nursing home) at 1 year	Higher age and urinary incontinence are independent predictors for nursing home as residence at 1 year
Wyller	To study gender differences in functional outcome and residency after 1 year in 65 stroke patients admitted to hospital within 14 days after the stroke	Gender was the only investigated prognostic factor	Place of residence (other home versus nursing-home) after 1 year	After one year males had a lower likelihood to be permanent nursing-home residents. Among patients not permanently institutionalized after one year, a significantly higher proportion of women than of men lived alone

BI: Barthel ADL Index, which measures activities of daily living and ambulation. **Constructional apraxia**: the ability to number a clock, copy a drawing of a house and copy dual pentagons. **MMSE**: Mini Mental Status Examination for cognitive impairment which includes orientation, memory, attention and language. **ASB**[19]: Assessment of Stroke and other Brain Damage for assessment of cognitive functions, which includes speech quality, language, auditory comprehension, ideomotor apraxia, ideational apraxia, visuospatial constructive subtest. **SMES**[20]: Sødring Motor Evaluation of Stroke Patients with subscores for arm, leg and gross motor function.

In Table 4 the prognostic factors with an unfavourable outcome for independent living in all ten studies have been ranked according to level of scientific evidence for the studies.

Table 4. Ranking of identified prognostic factors in relation to level of scientific evidence for the studies (numbers correspond with the references)

Prognostic factors	**Level A**	**Level B**
Low initial BI score at day seven	12	1,2,13
High age	17	13
Low MMSE score	12	13
Paresis of arm and leg	12	14
Not alert as initial level of consciousness	12	
Old hemiplegia	12	
Homonymous hemianopia	12	
Visual extinction	12	
Constructional apraxia	12	
No transfer to the stroke unit	12	
Non-lacunar stroke type	12	
Visuospatial construction problems	16	
Urinary incontinence	17	
Female gender	18	
Not married/not living with someone else		2,13,14
Low SSS score		1,15
Bad initial orientation		2
Low MMAS score		13
Low CNS score		13
Unawareness of illness		14

SSS: Scandinavian Neurological Stroke Scale, which evaluates level of consciousness, eye movement, power in arm, hand, and leg, orientation, aphasia, facial paresis, and gait. **MMAS**: Modified Motor Assessment Scale, which consists of eight motor activity items. **CNS**: Canadian Neurological Scale, which monitors mentation, motor function and motor response.

Discussion:

It is remarkable, that despite the large number of studies about prognosis in stroke so few studies satisfied the inclusion criteria of our literature search. The main reason is that few studies were performed with future residence as outcome measure. But perhaps interest in this topic is increasing, as all the studies included in this review date from 1995 or later. Besides many articles were excluded because follow-up was too

short, often three months or less. Since substantial recovery is possible[21] from three to six months after stroke at least six months follow-up is recommended.[22,23] Also an unclear and unexplained selection of patients presumably resulting in heterogeneous populations led to exclusion of many articles, because if the selection criteria have not been unambiguously specified, a valid basis for generalisation of prognostic results is lacking. Owing to the strict inclusion criteria the prognostic factors from this review are only valid for application within the first two weeks post-stroke, and for prediction of the future residence during six months to one year. Factors with high predictive quality in the first two weeks post-stroke could have different predictive quality in a later period, e.g. during the treatment in a rehabilitation center. Pooling the results of this review in a meta-analysis was not possible, because no raw data were available, and the tables in the studies did not provide sufficient information. Furthermore heterogeneity across studies was huge. None of the studies in this review described a conceptual framework as basis for the choice of the examined prognostic factors. The best evidence synthesis of level A articles results in the following prognostic factors with an unfavourable outcome for independent living after one year (see Table 4): Amongst biology/disease factors we found high age, female gender, and non-lacunar stroke type. The somatic disturbances of functions /structures were paresis of arm and leg, old hemiplegia, homonymous hemianopia, and urinary incontinence, and at activities level low initial ADL functioning. With regards to cognitive disturbances at the level of functions/structures were found: not alert as initial level of consciousness, visual extinction, constructional apraxia, and visuospatial construction problems, and at the level of activities low MMSE score (i.e. disturbances in orientation, memory, attention and language). At organisational level this was absence of a transfer to the stroke unit. So the majority of the identified prognostic factors comes

from lesions in functions and structures, and apart from somatic disturbances cognitive disturbances seem to be of major importance for the ability to live independently.

To predict the future residence at the time of hospital discharge insufficient evidence exists for all the investigated prognostic factors from this review, since no factor was demonstrated in at least two level A studies, our standard for scientific evidence.

Although few studies could be found concerning this topic their methodological quality was remarkably good with scores from seven to nine out of eleven (see Table 2). But even articles of level A with a high methodological score showed methodological flaws. E.g. quality and quantity of medical and paramedical interventions (item J) were not reported in the studies of Friedman and Sveen et al., but could have influenced results. Because in the study of Thommessen et al. external validity (items I, J and K) had not been assessed, there was insufficient insight into patient characteristics, and the criteria for admittance to the geriatric ward were not specified. In the study of Wyller et al. chance could have contributed to the results of this study, because a post-hoc hypothesis on unexpectedly found gender differences has been investigated. Furthermore, bias could have been introduced by the fact that older female stroke patients, already permanently institutionalized, had received a higher threshold for referral to hospital. The validity of prediction was questionable in some level B studies[,], in which statistical modelling (items F and H) was absent or insufficient.

Contradictory results in this systematic review were the predictive value of the BI in the study of Friedman, and the absence of it in the study of Thommessen. Likewise age had predictive value in the study of Thommessen, but not in the study of Friedman. MMSE was a predictor in the study of Friedman, but not in the study of Thommessen, and gender had predictive value in the study of Wyller, but not in the study of

Friedman. Explanations for contradictory results could be the differences between study populations, and the differences in size and power of the studies. By means of post-hoc power analyses, indeed we could show that some of the studies had too little power to prove prognostic value for the investigated factors, while for other factors insufficient information was available in the studies to be able to make a power calculation. But the effect sizes of the BI and MMSE in the study of Friedman, of age in the study of Thommessen, and gender in the study of Wyller seemed to be substantial.

In the absence of a conceptual framework the risk is huge that important prognostic factors are missing, and surrogate prognostic factors are included. For example, because the biologic factors gender and age are indicator variables with a huge joint variable portion, they could code for other factors like comorbidity or social factors, if these factors have not been seperately investigated and put into the model for statistical analysis. One solution for this problem is research based on a conceptual framework with investigation of all relevant prognostic factors in a population with sufficient sample size and cross-validation in other populations. Only then we can clearly understand the clinical meaning of the statistical results.

From clinical practice we know that besides prognostic factors for the future level of functioning in ADL and ambulation social factors also can be important for the chances to live independently six to twelve months post stroke. Yet, contrary to clinical experiences this systematic literature search did not reveal any prognostic factors from the social domain (in only three level B studies'' the social factor marital status had been investigated). The main reasons for this absence seem to be that few studies were performed with future residence as outcome measure, that most of the identified studies did not meet the inclusion criteria of this systematic review, and that in few of the selected and non selected

studies a social factor had been investigated. However, although epidemiological studies have reported about the importance of social factors for reducing risk of mortality from a wide range of causes[24,25] (so these factors do not seem to be stroke specific) and although stroke studies[26,27,28] have reported models with social support as predictor of discharge destination and institutionalization, scientific evidence for this last thesis is insufficient.

Furthermore, in order to live independently in one's own home, especially without social support, more functions and activities will be needed over those needed for independence in ADL and ambulation. E.g. sufficient cognitive and communicative abilities to be able to handle one's own affairs could be important. Indeed, in this review we found many prognostic initial cognitive disturbances with a negative influence upon the future ability to live independently.

Conclusion

Insufficient scientific evidence exists for the clinical meaning of all the identified prognostic factors from this review, since no factor was demonstrated in at least two level A studies, our standard for scientific evidence. None of the studies in this review described a conceptual framework as basis for the choice of the examined prognostic factors. The best evidence synthesis of level A articles results in the following prognostic factors with an unfavourable outcome for independent living after one year: high age, female gender, non-lacunar stroke type, paresis of arm and leg, old hemiplegia, homonymous hemianopia, urinary incontinence, low initial ADL functioning, not alert as initial level of consciousness, visual extinction, constructional apraxia, visuospatial construction problems, low MMSE score, and absence of a transfer to the stroke unit. As this systematic literature search did not reveal any prognostic factors from the social domain, we conclude that in scientific

research until now social factors and their contribution to the possibility of living independently six to twelve months post-stroke have not or at least less well been investigated.

IMPLICATIONS FOR FURTHER RESEARCH

As scientific evidence is insufficient more research is needed into prognostic factors of the future residence in the subacute phase after stroke. More research is needed at the level of activities, but apart from research into prognostic factors at the level of activities of daily living and ambulation especially research regarding the importance of the social situation should be performed. A conceptual framework including prognostic factors from the clinical domains disease/biology, functions/structures and activities, as well as factors from the social domain should form the basis of this research.

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Clinical messages

- scientific evidence for prediction of the future residence is insufficient
- social prognostic factors have not or at least less well been investigated
- a conceptual framework as basis for the choice of the investigation of prognostic factors is needed

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Chapter 4

Prognostic social factors in the subacute phase after a stroke for the discharge destination from the hospital stroke-unit
A systematic review of the literature

Disability and Rehabilitation 2004; 26 (4): 191-197.

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Abstract

Purpose*:* The objective of our study was to identify prognostic social factors in the subacute phase after stroke for the discharge destination from the hospital stroke-unit.

Methods: A systematic literature search was performed, designed in accordance with the Cochrane Collaboration criteria. Internal, statistical and external validity of the studies were assessed using a checklist with 11 methodological criteria.

Results: Characteristics of the social situation that proved to be important for prediction of the discharge destination are marital status and social support. Quantity and methodological quality of the research studies were insufficient, and the number of possible social prognostic factors investigated was limited by the absence of a conceptual framework of social subdomains in the studies, including an unambiguous definition of the prognostic social factors within these subdomains.

Conclusions: A great need exists for research into the prognostic qualities of the following social factors: the ability to provide support, presence, and readiness of the homefront; the availability of professional care, personal financial means, membership of societies and clubs, frequency of contacts with close relatives and friends; the quality of the patient's residence with regard to the adaptation to the needs and abilities of the patient. A commitment about the aforementioned conceptual framework is mandatory.

Keywords: prognosis, social situation, discharge destination, stroke-unit, systematic review.

Introduction

Apart from stroke outcome measurements like mortality, impairments, disability, quality of life, and length of hospital stay, other measurements like discharge destination and future (id est six to twelve months post-stroke) residence are also important. Recovery after a stroke is influenced by many factors, including psychosocial ones. Social support is a complex and multidimensional concept and can affect disease susceptibility, course of illness, compliance with treatment, rehabilitation, and mortality[1]. Moreover, the presence of social support could be an important predictor of discharge destination[2,3]. In many cases the success of a return home is probably more affected by the characteristics of the primary caregiver, than by the characteristics of the stroke patients themselves. Unsworth et al.[4,5,6] analyzed the accommodation recommendations and policies of 13 rehabilitation teams. Out of 15 prognostic factors, a patient's mobility status, their ability to perform personal ADL tasks, and their social support were central for the decision of the discharge destination. In her study concerning admission to rehabilitation centers, Haas[7] considered medical and non-medical prognostic factors and strong family support was a positive non-medical factor. Flick[8] mentioned medical status, functional status, mental status, physical endurance, and social support as prognostic factors in determining the rehabilitation setting. Unfortunately , neither of the above mentioned studies described a framework with a clear motivation of the choice of the examined prognostic factors, nor has an unambiguous definition of the social factors been presented. With regard to a conceptual framework we are of the opinion that the prognostic social factors should be divided into the social subdomains homefront, social situation, and residence[9]. The homefront exists of the spouse and/or other important persons who live together with the patient. The social situation of the patient encompasses his personal financial

means, the availability in the society of professional care, and the quality of his social network. The residence should be adapted to the needs and abilities of the patient, and be well approachable and accessible. But which supportive factors of the homefront and the social situation and which other social factors might be important for the decision of the discharge destination from the hospital stroke-unit is as yet unknown. This is the reason for the current literature search to identify these prognostic social factors. Our research question is: which social factors could have a predictive value for the decision of the discharge destination from the hospital stroke-unit?

Methods

SEARCH STRATEGY

In accordance with the Cochrane Collaboration criteria[10] we performed a literature search up to March 2003 for all studies published in English, German, French and Dutch for prognostic social factors of the discharge destination from the hospital stroke-unit. Keywords were stroke, patient/hospital discharge, social support/situation/environment, housing, home care services, finance. Information sources were Medline, Embase, Cinahl, Current Contents, Cochrane Database of Systematic Reviews, Psyclit, Sociological Abstracts, reference lists, personal archives, consultation of experts, Guidelines of the Netherlands Society for Neurology (1996)[11], Guidelines Stroke 2000 of the Dutch Institute for Quality in Health Care CBO[12], The Scottish Intercollegiate Guidelines Network Management of patients with stroke (2002)[13], The English Royal College of Physicians National Clinical Guidelines for Stroke (2002)[14], and The Guidelines of the National Institute of Neurological Disorders and Stroke of the U.S. National Institutes of Health (2001)[15]. The full search strategies are available from the authors.

SELECTION CRITERIA

Inclusion criteria: cohort and randomised clinical trial studies including patients with an ischemic or haemorrhagic stroke, and an assessment of prognostic factors at the hospital stroke-unit, in which at least one social item was investigated, and the discharge destination was taken as outcome measurement. Because of the potential importance regarding the decision of the discharge destination, we additionally selected studies which used future residence and future ADL functioning (6 to 12 months after stroke) as outcome measures.
Exclusion criteria: case studies, case series and non-systematic review articles; all studies which included patients with a transient ischemic attack (TIA), in which a separate analysis of patients with stroke is not possible; subarachnoid hemorrhage.

METHODOLOGICAL PROCEDURE FOR VALIDITY ASSESSMENT AND DATA ABSTRACTION

All relevant publications were tested for internal, statistical and external validity according to the 11 methodological criteria as explicated in the systematic literature review of Kwakkel et al. (1996) [see Appendix][16]. These methodological criteria have been recommended by the "Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap"[17] in order to improve the scientific quality and comparability of stroke outcome research. The criteria are in agreement with the general recommendations for studying prognosis in this field[18,19], and can be applied to clinical trials as recommended by the Cochrane Collaboration, as well as to other kinds of research such as cohort studies, which form the majority of studies in this field of research.
A binary weight (0/1) was given to each of the 11 methodological criteria listed in table1. All prognostic studies were scored according to these criteria by two reviewers (RM, JvL). Any disagreements were resolved by discussion or, if necessary, by consulting a third reviewer. Finally we

classified the publications included in this review according to level of scientific evidence, where A means good, B moderate, and C poor evidence (see table1). Studies that satisfy all items for internal and statistical validity (≥ 8 points) received level A, studies with a total score > 6, but not fulfilling the criteria for level A received level B, and studies with a total score ≤ 6 received level C. Like Kwakkel et al. we gave a higher value to internal and statistical items.

Results*:*

From the initially identified 190 studies, we selected 13 publications on the basis of the title and the abstract. In case of uncertainty regarding the inclusion, the entire text of an article was read. Six articles, all cohort studies involving a total of 929 patients, were selected for the systematic review. The number of patients included in the studies ranged from 46 to 524. These articles were then evaluated according to the 11 criteria as presented in the Appendix . The results of the methodological scoring are summarized in table 1.

Table 1. Methodological assessment

				Internal validity					Statistical val.			External val.			Score	Level
1st author	**Year**	**ref**	**N**	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**	**max 11**	
Brosseau	1996	20	152	1	1	0	0	1	1	0	1	1	1	0	7	B
Colantonio	1993	21	87	1	1	1	0	1	1	0	0	1	0	0	6	C
Geerts	1995	22	63	1	1	1	1	1	1	0	0	1	1	0	8	B
Glass	1993	23	46	1	1	1	1	1	1	0	1	1	0	0	8	B
Jehkonen	2001	24	57	1	1	1	1	1	1	0	1	1	0	0	8	B
Pedersen	1996	25	524	1	1	1	1	0	1	1	1	1	1	0	9	B

Year: year of publication; Ref: reference number in the text; N: number of patients recruited in the study; A to K: criteria for methodological score as described in Table I; Score: total score of A to K; Level: level of scientific evidence (see text).

As shown in table 1, the following classifications for the level of scientific evidence were found: five level B , and one level C. No studies cross validated their results in an independent second study (item K). All studies fulfilled the criteria for valid and reliable measurements of dependent and independent factors, for statistical testing of the relationship between dependent and independent factors, and for specification of relevant patient characteristics (items A, B, F, and I). The results from the studies are summarized in table 2.

In all the six studies of this systematic review the social domainof the patient was of major importance. Social support, presence of a relative at home, and marital status predicted discharge residence. Larger social networks and living with someone else predicted risk of institutionalization post-rehabilitation. Larger social networks and perceived social support also predicted better physical function. None of the studies selected for our systematic review described a framework of social subdomains with a clear motivation of the choice of the examined prognostic social factors.

Table 2. Results of the articles.

First author/ Level study	Purpose of the study and Population	Prognostic factors	Outcome factors	Main results
Brosseau et al. Level B	To identify predictors of discharge disposition after an acute stroke rehabilitation program in a general hospital in a cohort of 152 patients	Age, gender, stroke type and site, post-stroke duration, medical complications, comorbidity; sensorymotor, cognitive-perceptional, communication, and functional status at admission; social support	Private home, rehabilitation center (rc), and long-term care facility(ltcf) as discharge residence	Compared with discharge to home low total FIM score at admission, bad social support, and gait status predicted discharge to a rc or a ltcf; presence of medical complications predicted discharge to a ltcf
Colantonio et al. Level C	To identify psychosocial predictors of physical function and institutionalisation in 87 elderly survivors of stroke in a prospective cohort	SNI, availability of social support, religiousness; pre-stroke CES-D, cognitive impairment, Katz ADL scale, Rosow scale; age, sex, race, education, housing type, comorbidity, stroke severity	Institutionalization, Katz ADL scale, and Rosow scale 6 weeks postdischarge from hospital	Larger social networks were associated with fewer limitations in physical function and with a lower risk of institutionalization
Geerts et al. Level B	To describe the routing of stroke patients through the health care system in the first year after stroke in 63 patients from a cohort of 145	Age, gender, marital status, place of residence, living circumstance (alone or with family), CNS, MMSE, BI, and MMAS	Place of residence six and twelve months after stroke	Patients living at home are younger, have higher scores on the MMAS, CNS, MMSE, and BI and are living with someone else
Glass et al. Level B	To examine the impact of social support on outcome in a prospective cohort study of 46 surviving first ever stroke patients	Stroke severity as scored by level of consciousness, and perceived social support as scored by the ISSB	Activities of daily living as measured by the BI at 5, 30, 90, and 180 days after stroke	Patients with more social support improved the most over time. Patients with moderate to severe stroke and high social support improved the fastest and continued to improve till 180 days
Jehkonen et al. Level B	To explore prognostic factors at the acute stage of stroke connected with the return to home in a prospective cohort of 57 right hemisphere stroke patients	Age, gender, size of infarct, neglect, hemiparesis, verbal memory, unawareness of illness, anosognosia for neglect, anosognosia for hemiparesis, and presence of a relative at home	Length of hospital stay, and returning home versus not returning home during a 1-year follow-up	Hemiparesis, unawareness of illness, absence of a relative at home lengthened the time from stroke to discharge to home, and increased the possibility of not returning to home
Pedersen et al. Level B	To determine the influence of ini-tially lowered orientation on dis-charge placement in 524 patients with acute stroke from a cohort of 896 patients	SSS; aphasia and orientation were assessed using the subscales for aphasia and orientation in the SSS. Initial BI, age, sex, comorbidity, prior stroke, and marital status	Discharge residence (independent living versus nursing home)	Initial orientation, initial BI and marital status predicted discharge residence

Abbreviations:
SNI: Social Network Index for assessment of marital status, contacts with close friends and relatives, participation in group activities, and church membership. **CES-D**: Center for Epidemiologic Studies Depression scale. **Katz** ADL scale: measures activities of daily living **Rosow** scale: measures higher levels of physical function. **MMSE**: Mini Mental Status Examination for cognitive impairment which includes orientation, memory, attention and language. **BI**: Barthel ADL Index, which measures activities of daily living and ambulation. **MMAS**: Modified Motor Assessment Scale, which consists of eight motor activity items. **ISSB**: Inventory of Socially Supportive Behaviors26 for measurement of emotional, instrumental, and informational perceived social support. **SSS**[27,28] : Scandinavian Neurological Stroke Scale, which evaluates level of consciousness, eye movement, power in arm, hand, and leg, orientation, aphasia, facial paresis, and gait. **FIM**: Functional Independence Measure for assessment of activities of daily living, ambulation, communication, and social cognition. **CNS**: Canadian Neurological Scale, which monitors mentation, motor function and motor response.

Discussion:

CONCERNING THE ABSENCE OF A CONCEPTUAL FRAMEWORK

Although literature about the social situation of the stroke patient is abundant, very little research has been performed to identify social prognostic factors for the discharge destination from the hospital stroke-unit during the subacute phase post stroke. This is also true for studies focusing on the impact of social factors on future residence and future level of ADL. Like the studies mentioned in the introduction, none of the studies selected for our systematic review described a framework with a clear motivation of the choice of the examined prognostic factors, nor has an unambiguous definition of the social factors been presented. Unfortunately, important items of the social subdomains have hardly been investigated and the following questions remain: Are the physical and emotional abilities and support of the homefront sufficient? Is the homefront willing to support the activities of daily life, household activities, and emotional problems? Is the presence of the homefront sufficient? Does the patient possess so much personal financial means that he or she is able to buy sufficient home care services and is professional care available? Is there a presence of a social network, which means being together with close friends/family once or more than once a week for longer than one hour, membership of and weekly active participation in activities of a club, or active membership of a religious community[21]? Are facilities and necessary temporary adaptations to the residence available or practicable within three months? All the above mentioned factors increase the chances of return to an independent living situation.

None of the selected six articles of this review reached a level A of scientific evidence. Pooling the results of this review in a meta-analysis was not possible, because no raw data were available. Furthermore

heterogeneity across studies was huge. All the articles showed considerable methodological flaws.

CONCERNING THE METHODOLOGICAL QUALITY OF THE ARTICLES

In the study of Brosseau et al. the time period post-stroke of the prognostic assessments ranged from one to 68 days with a mean of 11 days and a standard deviation of 15 days. This implies that many of the first assessments took place after day 14 and this is too late for early determination of a prognosis (validity item C). The outcome assessment took place at the time of discharge from the stroke unit and ranged from five to 173 days after admission. In most cases this time was less than six months after stroke and this is not an appropriate end-point for observation (validity item D). In the study of Colantonio et al. the outcome assessment took place six weeks post discharge from hospital, but the period of time post stroke has not been mentioned. This could introduce selection bias, because patients can be discharged from hospital at different times post stroke. Moreover, six weeks post discharge from hospital is not an appropriate end-point for observation (validity item D). In the study of Geerts et al. selection bias could have been introduced, because the patients in the study group of 63 patients, in which 79% of the patients lived at home, while only 2% lived in a nursing home, are a positive selection compared with the patients in the drop-out group, in which 28% lived at home and 26% in a nursing home. Glass et al. used level of consciousness as instrument to determine stroke severity, which to our opinion is not a valid way to indicate stroke severity. Furthermore, the study suffers from a small sample size (validity item G). Although in the study of Jehkonen et al. the unawareness of illness recovered rapidly (all of the patients were aware of the illness at the 3-month follow-up), this is nevertheless most probably an indicator of a severe stroke increasing the likelihood of a poor outcome. As Pedersen et al. reported

in their study orientation for time, place and person is a crude measure of intellectual function. If apart from an assessment of orientation also assessments of other cognitive functions such as memory and attention would have been performed and analyzed in a multivariate regression model, this could have given a better idea of the prognostic value of orientation by itself on discharge placement.

CONCERNING THE RESULTS

Which characteristics of the social domain proved to be important for prediction? In the study of Glass et al. patients with more social support physically improved the most over time. In the studies of Jehkonen et al. and Pedersen at al. the presence of a relative at home and marital status influenced discharge residence, and in the study of Geerts et al. living with someone else influenced future residence. In the study of Colantonio et al. larger social networks (and not different types of social support) were associated with fewer limitations in physical function and with a lower risk of institutionalization. So in the studies of this systematic review the social domain of the patient, especially the presence of a relative at home, seems to have an independent effect on institutionalization. This finding confirms the notion that social factors, notably marital status and a large social network, as well as health factors play a role in the decision of the discharge destination from the hospital stroke-unit and in nursing home admissions. In an ageing society these social factors are of growing importance. Limitations of this review are caused by the small number of the studies selected, the weak methodological quality such as the small sample size of all studies with the exception of the study of Pedersen et al. (see item G in Appendix and table 1), and the limited number of social prognostic factors investigated caused by the absence of a conceptual framework in the studies.

Conclusion

In the studies read for this review characteristics of the social situation that seemed to be important for prediction of the discharge destination are marital status and a large social network with social support. Notwithstanding our clinical experience and the results from this systematic review concerning the importance of social factors for prediction of the discharge destination from the hospital stroke-unit, insufficient scientific evidence exists for all the investigated prognostic factors from this review, since no factor was demonstrated in at least two level A studies, our standard for scientific evidence. Moreover many possibly relevant factors have until now not been investigated in the subacute stage of stroke.

IMPLICATIONS FOR FUTURE RESEARCH

Based on the results from this systematic review we advise that in future studies prediction models for the discharge destination from the hospital stroke-unit should not only contain clinical factors, but also social factors. Like for the clinical factors the social factors need a conceptual framework similar to the one we presented in the introduction, including un unambiguous definition of the factors of the social subdomains.

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Appendix

Binary outcome strategies rated "adequate" (Kwakkel et al.)

Outcome strategies	**Criteria**	**Criterion in Table 2**
To evaluate internal validity		
Measurements reliable and valid? Dependent variable	Positive, if the prognostic study tested the reliability and validity of measurements used or referred to other studies which had established reliability and validity	A
Measurements reliable and valid? Independent variable		B
Inception cohort during observation period	Positive, if observation started within 2 weeks after stroke	C
Appropriate end-points for observation?	Positive, if observation ended a minimal of 6 months after stroke	D
Control for drop-outs?	Positive, if drop-outs durirg period of observation are specified	E
To evaluate statistical validity		
Statistical validation of relationship between dependent and independent variables?	Positive, if relationship between dependent and independent variable is tested for statistical significance	F
Sample size (n) adequate in relation to the number of determinants (K)?	Positive, if ratio n : K exceeds 10 : 1	G
Control for multicollinearity?	Positive, if relationship between two or more independent variables is tested in the prediction model	H
To evaluate external validity		
Specification of relevant patient characteristics? (i.e. age, type, number and localization of stroke)	Positive, if age, type, localization as well as number of strokes are specified in the cohort	I
Description of additional medical and paramedical interventions during observation?	Positive, if information on medical and paramedical treatment was reported	J
Cross-validation of the prediction model in a second independent group?	Positive, if the prediction model is validated in a second independent group of stroke patients	K

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Chapter 5

The use of a Modified Delphi procedure for the determination of 26 prognostic factors in the subacute stage of stroke

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Abstract

The aim of this study was to reach consensus about the prognostic factors when deciding the discharge destination from a hospital stroke unit, and to construct a prognostic conceptual framework. To realise an optimal integration of knowledge from research findings and from clinical experience by expert opinions we used a "modified Delphi Technique", which is the most commonly used method for the production of clinical guidelines. As result the process yielded 26 prognostic factors, which were arranged in clinical and social subdomains. The subdomains and the factors within each subdomain were prioritized according to their assumed predictive value for the decision process. The order of importance of the prognostic factors of the clinical domain was: 1. disabilities, 2. premorbid disabilities, 3. impairments, 4. disease/biology; and the order of importance of the factors of the social domain was: 1. homefront, 2. social situation, 3. residence. The Delphi procedure is an excellent instrument to determine and prioritize prognostic factors. With this procedure research-based and consensus-based knowledge can be combined. For a valid procedure it is mandatory to state explicitly in advance how the scores will be judged, and to explain the scientific level of the evidence during the whole procedure.

Introduction

Stroke represents a major burden of sickness and reduces the quality of life for patients and their carers. Because of the multitude of symptoms in many crucial functions such as sensorimotor, cognitive and communicative functions stroke may cause serious threats for the abilities of the patients to remain independent in self-care or to be able to live independently with or without support. The financial costs for the community are substantial.

The aim of stroke-units is to increase quality of care by among other things multidisciplinary treatment of specialists in stroke and by participation in a regional transmural stroke-service chain. Stroke patients who receive organised inpatient care in a stroke unit are more likely to be alive, independent, and living at home one year after the stroke[1].

Planning the discharge destination from the hospital stroke unit is a major step in choosing an optimal rehabilitation care route for the individual patient[2]. However, there is a variation in clinical practice regarding the decision of the discharge destination in The Netherlands and abroad, and the Stroke Guidelines 2000 of the Dutch Institute for Quality in Health Care CBO [3] do not contain any discharge guideline.

The prognosis of a stroke and the subsequent planning of a discharge destination are very difficult subjects. Fortunately the body of knowledge about the factors which determine the decision to discharge is growing. In reaching this decision clinical and social prognostic factors for future functioning in activities of daily life and ambulation[4], and for the future residence[5,6], as well as the available local discharge destinations are of paramount importance. However, the present research evidence base for these prognostic factors is incomplete and the scientific level of evidence is insufficient. This is not surprising, because apart from methodological flaws in the studies, none of the studies we examined described a conceptual framework as a basis for the choice of the prognostic factors that were examined in these studies. Until now, without a systematic view, the amount of prognostic factors investigated constitutes an amorphous mass for any unwary researcher.

This article reports on the process that led to the determination of 26 potentially relevant prognostic factors based upon evidence derived from systematic reviews and supplemented by expert opinions. We intend to analyse these factors in a recently started multicenter prospective cohort

study so that subsequently they will form the basis for the development of an evidence based guideline for the decision of the discharge destination from the hospital stroke unit.

Methods

SOURCES OF EVIDENCE

To identify potentially relevant prognostic factors for the level of activities of daily living and ambulation, and the residence at six to twelve months after stroke that could be of importance when deciding a discharge destination, we performed three systematic literature searches, designed in accordance with the Cochrane Collaboration criteria[7].

All relevant publications were tested for internal, statistical, and external validity according to 11 methodological criteria, which are in agreement with the general recommendations for studying prognosis in this field[8,9]. According to these criteria the publications were divided into four levels of evidence (A to D), and depending on the number of A and/or B publications as basis for the theses posed below, these theses were divided into four levels of evidence (1 to 4) in accordance with the recommendations of the Guidelines Stroke 2000 (see Table 1).

Table 1. Level of evidence of the theses

Level	Criteria
1	If supported by at least 2 mutually independently executed studies of level A [i.e. studies that satisfy all items for internal and statistical validity (≥ 8 points out of 11)]
2	If supported by at least 2 mutually independently executed studies of level B (i.e. studies with a total score > 6, but not fulfilling criteria for level A), or by 1 study of level A
3	If supported by at least 1 study of level B (no support by a study of level A)
4	If not supported by a study of level A or B (i.e. studies of level C with a total score ≤ 6; or level D expert opinion, based upon knowledge and experience)

FORMAL CONSENSUS

To realise an optimal integration of knowledge from research findings and from the clinical experience of experts, contacted over the internet, we performed a "modified Delphi Technique", which has been developed by the RAND corporation[10]. This is the most commonly used method for clinical guideline production[11]. This is a formal consensus development method which consists of two or more postal rounds and a final consensus meeting, which allows participants to discuss issues face to face. The process has a structured format and the "voting" is anonymous. The main characteristic of a Delphi procedure is the structured forming of an opinion by repeated feedback of information.
The design of our research is presented in Table 2.

Table 2. Design of the research

1.	Systematic reviews
2.	Clinical experience of research group
3.	Formulation of list of influential facors
4.	Assigning level of scientific evidence to the factors
5.	Modified Delphi procedure
a.	2 postal rounds - scoring of factors - presentation of new factors
b.	consensus meeting - scoring of factors - construction of a theoretical framework with arrangement of prognostic factors in domains - giving priorities to the domains and the factors within the domains

PROCESS

Panel

A panel of 23 members, representing the key disciplines of the transmural stroke service chain nationwide was formed, including physiatrists, neurologists, general practitioners, nurses, physiotherapists, social workers, nursing home care managers, home care managers, and policy managers. The members of this panel reflected the full range of professionals to which the guideline will apply and they were asked to participate because of their recognised authority in transmural stroke care, and their intention to commit to the process.

Theses

For the modified Delphi procedure the project leader (RM) presented 57 "influencing factors" based upon potentially relevant prognostic factors gleaned from literature and clinical experience of the research group. These were presented to the panel members for judgement. A booklet was compiled containing these 57 factors (each having been assigned a scientific level score) [see Table 1]). Furthermore, a complete reference list of literature was presented. Each potential influencing factor had to be rated on a 5 point Likert scale, with scores ranging from most agreement to least agreement (see Table 3 for an example). Apart from rating these factors, the panel members were asked to comment on their rating choices.

Table 3. Part of a score form for rating the "influencing factors"

Urine incontinence post stroke has a negative influence upon the final level of functioning [scientific level 1]				
Completely agree	Agree	Doubt	Disagree	Completely disagree
Comment:				
Loss of consciousness within the first 48 hours post stroke has a negative influence upon the future possibility to live independently [scientific level 2]				
Completely agree	Agree	Doubt	Disagree	Completely disagree
Comment:				

Digital postal rounds

In our modified Delphi procedure two postal rounds were completed before the consensus meeting took place. the exchange of information and ratings between the researchers and the panel members was performed over the internet[12].

An ICT company functioned as a link between researchers and panel members. The researchers sent the booklet with the factors and scoring list to the company, which in turn forwarded them onto the panel members. The panel members filled in the scoring list and commented ontheir ratings and returned them to the company. The company gathered the information, deleted the address of the sender and then sent everything back to the researchers.

The researchers summarised the arguments per factor and calculated the frequency of response to each factor presented. The pattern of responses of the whole panel (see Table 4), the individual scores, and the summarised arguments for each factor were presented in the second

round of the Delphi procedure. The complete scoring lists are available from the author.

Table 4. Example of a response pattern for the whole panel (P) compared to an individual response (I) for two "influencing factors" (%)

Theses	Completely agree	Agree	Doubt	Disagree	Completely disagree	Number missing
Urine incontinence P	20	60	15	5	0	1
Urine incontinence I		X				
Loss of consciousness P	16	37	37	10	0	2
Loss of consciousness I	X					

So the panel members were allowed to see the spread of agreement and how their own response related to this.
Besides giving arguments for their responses to the factors, the panel members were asked to mention other factors that were not represented first time round , but which, in their opinion, could be of importance when deciding on appropriate discharge destinations for stroke patients.

Consensus meeting

The multidisciplinary panel for the consensus meeting comprised 12 members, among whom all the key disciplines were represented. This group was not too large to cause coordination problems, and not too small to diminish reliability[13]. The presence of all the key disciplines ensured that the whole spectrum of opinion and expertise were involved in the discussions[14,15]. An independent process leader (JL), was an experienced Delphi round facilitator, who let the process run smoothly and ensured that good quality, unbiased decisions were made. Also

present were the project leader (RM), two researchers (RM, DI), a secretary, and an independent process guard.
Because the aim of the research was to gather potential prognostic factors which would facilitate the decision-maing process when considering discharge destinations from a hospital stroke unit, the factors concerning the same prognostic factor for the future functioning and the future residence were combined and reformulated after discussion by the panel. For example, the two statements "Apraxia has a negative influence upon the final level of functioning" and "Apraxia has a negative influence upon the possibility of living independently" were combined to be "Apraxia has a negative influence upon the final level of functioning and the possibility of living independently".
The next step for the process leader and the panel was to construct a conceptual framework out of the accepted factors, in which the prognostic factors had been arranged into clinical and social sub-domains; a sub-domain being formed by two or more related prognostic factors. Subsequently scoring took place to prioritise the sub-domains and the prognostic factors within each sub-domain concerning their assumed predictive value for the discharge decision.
A secretary drew up the minutes during the meeting and after the meeting made a full report, including the followed procedures, the results of the voting rounds, the course of the discussions, and the final results. The independent process guard ensured that all procedures ran according to rules, that voting was truly anonymous and that the editing of the scores had been done correctly.

Analysis of thesis responses
During the Delphi rounds scoring took place on a five point Likert scale, which gave panel members the opportunity to give a differentiated opinion. For the final acceptance of the factors the scale was used as a

three point scale. In the consensus meeting scoring took place on a three-point Likert scale, because the discussion was used for differentiation of the opinions, and the goal of the scoring was acceptance of a thesis or its rejection.

The cut-off percentage for acceptance or rejection of a factor was set in advance at ≥ 75% consensus.

Results

The results of the Delphi procedure have been presented in Table 5.

Table 5. Results of the Delphi scoring procedure

	Influencing factor				
	Presented	Not accepted	New	Rejected	Accepted
Start of the procedure	57				
In 1st Delphi round	57	29 + 8		0	28
In 2nd Delphi round	37	13 + 0		18	6
In consensus meeting	13	5	0	0	8
Total					42
Total after reformulation					**26**

In the second to sixth column the numbers indicate the number of factors, which were presented, not accepted, newly formulated, rejected or accepted; in each new round the not accepted and the new factors were presented again. Accepted or rejected: ≥ 75% consensus; not accepted: < 75% consensus concerning acceptance or rejection; new: newly formulated theses.

In both Delphi rounds the results had been based upon 21 sets of answers. The answers from two panel members were excluded from analysis, because their answers had been received after the deadlline. In the consensus meeting the results were based upon 12 responses out of 12. Finally 26 prognostic factors were accepted, and these were further subdivided into cllinical sub-domains "pre-morbid situation, disease/biology, impairments, and disabilities", and into social sub-domains "homefront, social situation, and residence" in order to construct a prognostic conceptual framework. Moreover priorities regarding the assumed predictive value for the decision process had been given to the sub-domains and to the prognostic factors within each sub-domain (see Table 6). During and after the consensus meeting the panel members stated the process had run satisfactorily, meaning that there had been enough time to discuss relevant issues, they felt that they had had the opportunity to express themselves freely and that they had contributed to the results of the meeting.

Table 6. Prognostic conceptual framework with priorities of the prognostic factors within the clinical and social sub-domains.

Prognostic factors of the clinical sub-domains	**Priority**
Disabilities (somatic, ADL, social, psychological, communicative)	
Severe functional disabilities post-stroke	1
Severe behavioral problems	2
Severe communicative disabilities	3
Cognitive disabilities	4
Disorientation in time and place	5
Pre-morbid situation	
Pre-morbid functional disabilities	1
Pre-morbid cognitive disabilities	2
Pre-morbid depression and/or fear	3
Impairments	
Poor sitting balance	1
Severe hemiparesis/hemiparalysis	2
Impairments in position and movement sense	3
Neglect	4
Apraxia	5
Depression and/or fear	6
Urine incontinence	7
Loss of consciousness (< 48 hours post-stroke)	8
Disease/biology	
Severe stroke (nature, localisation, size)	1
Former stroke	2
Age (> 70-75)	3
Prognostic factors of the social sub-domains	
Homefront	
Abilities/supporting power	1
Readiness	2
Presence/availability	3
Social situation	
Availability professional care	1
Presence social network	2
Personal financial means	3
Residence	
Adapted to the needs and abilities of the patient	--

Priority: priority concerns the order of importance for the decision process; Sub-domain:a sub-domain has been formed by two or more related prognostic factors.

Discussion

The Stroke Guidelines 2000 of the Dutch Institute for Quality in Health Care CBO contain important indications for improving the quality of care. To match the type of patient with content and place of care was not an issue, and the Guidelines do not contain any advise on deciding a discharge destination from a hospital stroke-unit. Based upon scientific evidence derived from systematic reviews of critically appraised research literature and supplemented by expert opinions we have determined 26 clinical and social prognostic factors that are potentially relevant for prognosis and choice of discharge destination. In the Delphi procedure an explicit linkage had been made between the evidence and the "influencing factor". Throughout the Delphi process all information was made available to the participantsso that they could see the spread of agreement and how their response related to this.
At present, we are validating the 26 identified prognostic factors in a prospective cohort study involving six stroke units nationwide.

Conclusions

Important items for assessing validity in the consensus development process concerning prognostic stroke studies are:

- to start with a solid scientific basis from systematic reviews of critically appraised literature
- participation in the panel of recognised authorities involving all key disciplines in stroke care
- making a link between the level of scientific evidence and the "influencing factors"
- giving the panel members the opportunity to add new factors based upon clinical experience, that were not mentioned in the original list as formulated by the guideline developer

- to construct a conceptual framework for categorisation of the prognostic factors
- leadership of an experienced Delphi round facilitator
- monitoring by an independent process guard
- evaluation during and at the end of the modified Delphi to ascertain that the panel members were happy with the process

Acknowledgements

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Chapter 6

Development of the Stroke-unit Discharge Guideline Choice of assessment instruments for prediction in the subacute phase post-stroke

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Abstract

The purpose of this paper is to present the design of an evidence based dataset of assessment instruments for the prognostic factors of the stroke-unit discharge guideline (SDG), a consensus based guideline for the decision of the discharge destination from the hospital stroke unit. In our systematic literature reviews and in known standard works we have looked for assessment instruments which are being used most frequently in stroke care, and subsequently we have searched for information regarding their validity and reliability. For 17 out of the 26 prognostic factors we found known applicable assessment instruments. Clinical feasibility and psychometric properties of most of these instruments is sufficient to good. For two factors we had to construct a new instrument. A simple definition was sufficient for the remaining seven factors. The SDG contains an evidence based dataset of prognostic factors and assessment instruments, and should be applied at the hospital stroke-unit, which is the first location to start with a uniform use of stroke assessment instruments. The SDG assessment instruments are part of the stroke service chain information system, which contains recently developed specifications for application in web based electronic patient records nationwide in the Netherlands.

Introduction

Because of the multitude of symptoms in crucial functions within the sensorimotor, cognitive and communicative domains, a stroke may cause serious threats for the patient, especially in his ability to care for himself and the capability to lead an independent life, either with or without support. After the acute stage of stroke for every patient a quick start of an optimal rehabilitation treatment program is of major importance. In

every country many treatment facilities exist, each with its own specific treatment modalities, and hence admission criteria.
The planning of the discharge destination from a hospital stroke-unit is mainly based upon the prognosis of future disabilities in daily life activities and ambulation, the prognosis of the future residence of the patient, and the presence of social support. Other factors are the therapeutic needs of the patient and patient preferences.
An evidence based discharge guideline could not be found in the literature. The lack of evidence based criteria that can be used to formulate the discharge destination from the hospital stroke unit is a problem, and uncertainty often exists about the correctness of the decisions taken[1]. Regarding the scientific base of prediction in stroke problems are manyfold. Many different outcome measures and outcome scales are in use. The start of the assessment in the stroke studies begins at varying times post-stroke, whereas an assessment within fourteen days post-stroke is mandatory for an early prediction at the hospital stroke-unit and to serve as a valid base for longitudinal data analysis. Furthermore, the outcome assessments take place at different times post-stroke, there is a variation in selected research populations such as restriction to a specific type of stroke or age period and few studies do exist with future residence as outcome measure. Apart from this, no studies could be found in which clinical and social factors have been combined into one prognostic framework. Systematic application of the recommendations of the "Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap"[2] is insufficient and few studies sufficiently meet criteria of methodological quality[3,4,5]. Moreover, differences do exist in clinical practice between countries and during a certain time period.
The aim of our research is to eventually develop a consensus based guideline for the decision of the discharge destination from the hospital

stroke unit based upon evidence derived from systematic reviews of critically appraised research literature, supplemented by expert opinions. We started our research with the performance of three systematic literature searches[3,4,5] designed in accordance with the Cochrane Collaboration criteria[6], to identify prognostic factors that could be of importance for the decision of the discharge destination. To realise an optimal integration of knowledge from research findings and from clinical experience by expert opinions we used a "modified Delphi Technique" developed by the RAND corporation[7], which is the most commonly used method for clinical guideline production. This modified Delphi procedure yielded 26 prognostic factors[8]. Subsequently, we constructed a conceptual famework, the Stroke-unit Discharge Guideline (SDG), in which the factors were divided into clinical and social sub-domains (see Table 1). Patient views or preferences are no part of the SDG. The purpose of the SDG is to give an objective advice to the patient with regard to the best rehabilitation route. Subjective preferences should be no part of this advice. Finally, the patient and the physician will decide to the definitive choice on the basis of the objective advice and personal preferences. To enable future scientific research and benchmarking in the stroke service chain also other information should be assessed routinely. So, although not part of the prognostic factors of the SDG type, size and localisation of the stroke (see www.stichtingmyosotis.nl under AMDAS) should be recorded, as well as demographic data such as gender, premorbid living situation, and institution that sent on the patient to the hospital. Furthermore, admission criteria of all the participating institutions of a stroke service chain should be specified.

Table 1 Framework of clinical and social prognostic factors

Prognostic factors of the clinical sub-domains
Disabilities (somatic, adl, social, psychological, communicative)
Severe functional disabilities post-stroke Personality disorder Severe communicative disabilities Cognitive disabilities Disorientation in time and place
Premorbid situation
Premorbid functional disabilities Premorbid cognitive disabilities Premorbid depression and/or fear
Impairments
Poor sitting balance Severe hemiparesis/hemiparalysis Impairments in position and movement sense Neglect Apraxia Depression and/or fear Urine incontinence Loss of consciousness (< 48 hours post-stroke)
Disease/biology
Severe stroke (nature, localisation, size) Former stroke Age (> 70-75)
Prognostic factors of the social sub-domains
Family circle
Abilities/supporting power Readiness Presence/availability
Social situation
Availability professional care Presence social network Personal financial means
Residence
Adapted to the needs and abilities of the patient

The various factors in the reported studies had been assessed using many different instruments. For future replication research we want to propose that one evidence-based dataset of prognostic factors and assessment instruments be used. In future, meta-analyses will then be meaningful. To measure the prognostic factors assessment instruments suitable for prediction are needed. This article describes the choice and in some cases the "development" of the assessment instruments for the 26 prognostic factors.

Methods

At the beginning of our research we determined the conditions the instruments should fulfill. Three types of considerations determine the choice of a suitable instrument: practical applicability, suitability for a specific target population, and psychometric qualities.

For application in the clinical setting at the hospital stroke-unit in the subacute stage of stroke the clinical feasibility of the instruments should be good, that is the instruments should be easily to apply, orderly, simple, patient friendly, and scoring should not be time consuming. Also aspects of validity and reliability as defined earlier[9] should be good.

PROCEDURE

At first we have looked for assessment instruments which are used most frequently in stroke care, and especially for instruments that have been used in our systematic literature reviews[3,4,5]. Furthermore, in standard works[10,11,12,13,14,15] and in the known literature we have searched for information concerning their validity and reliability.

Subsequently, with regard to factors for which no suitable assessment instrument could be found, we used items from known instruments; if this could not be done, we tried to make the clearest and most specific definition of the item as possible, based upon our clinical observations and experience.

Results

For most of the factors we could use known instruments that also had been found in the research literature. Because no suitable instruments that conformed with our conditions could be found to assess the premorbid cognitive disabilities and the presence of a social network, we constructed the heteroanamnesis list cognition (HAC) and the social network score (SNS) respectively for these factors (see www.stichtingmyosotis.nl under AMDAS). For the HAC we used the items of the Mini Mental Status Examination (MMSE)[10,11,13 ,16,17,18,19] and scored them retrospectively via heteroanamnesis. The quantification of the scores has been made on the basis of clinical relevance, that is: the presence of premorbid cognitive problems, the help requirement with activities of the patient, or even the need for professional therapy. The SNS has been derived from the social network index (SNI)[20], a structural index of social ties, which includes assessments of marital status, contacts with close friends and relatives, participation in group activities, and church membership. The items of the SNS are frequency and duration of contacts with close friends or relatives, active membership and participation in a society, or in a religious community. Scoring is simple and not time consuming.

The clinical item of personality disorder and the social items of readiness and presence of the family circle, availability of professional care, personal financial means, and adaptation of the residence have been clearly defined (see www.stichtingmyosotis.nl under AMDAS).

Table 2 provides a detailed survey of each of the SDG instruments, including (1) number of items, average time to complete, and completion of the list by the subject versus an assessment by an observer; (2) domains that were assessed and their scores; and (3) psychometric data (reliability and validity).

The Barthel Index[10,21,22,23,24,25] measures basic activities of daily living (ADL) in terms of mobility and self-care. It is the most widely used ADL scale and its psychometric properties have been extensively investigated.
The Aachen Aphasia Test[26,27] consists of six parts and its psychometric properties have been extensively investigated too. For predictive purposes at the stroke-unit we only use the section about communicative behaviour of the spontaneous production of language. This section describes the level of understanding of the produced language, and the possibility of a conversation about simple or complex items.
The Mini Mental Status Examination (MMSE)[10,11,13,16,17,18,19] assesses orientation, registration, attention and calculation, recall and language. A disadvantage of the MMSE is that it attempts to compress assessment of too many functions into one test. For interpretation it is essential to consider the profile of the domain scores, and not just the overall total score. Apart from insensitivity to specific cognitive deficits such as those concerning visuo-spatial and perceptual abilities, the test is also notoriously insensitive to frontal lobe disorders such as the ones concerning executive and social functions. Nevertheless it is one of the most commonly used brief mental tests.
The Center for Epidemiologic Studies Depression Scale (CES-D)[13,28] is one of the most widely used depression scales. It should not be viewed as a diagnostic tool, but rather as a screening test to identify persons at risk of depression. A limitation is that it cannot distinguish between primary depressions and secondary depressions, caused by other factors than stroke-related ones. Furthermore, it may fail to separate depression from generalized anxiety and may not distinguish past from present disorders.

Table 2 Summary of psychometric properties of the SDG assessment instruments*

Instrument	Length/time (min)/rater	Domains/scoring
Barthel Index (BI)	10 items / 5-20 / interviewer-observer	Measures acitivities of daily living and ambulation / 1 summated total score
Aachen Aphasia Test (AAT)	6 items / 2 / observer	Communication level by language / 1 score
Mini Mental Status Examination	30 items / 5-10 / interviewer	Screening test for orientation, memory, at-tention and language/ best to study the actual respons to each domain, not the total score
Hetero Anamnesis Cognition	30 items / 5 / caregiver	Same items as MMSE / 1 score
Center for Epidemio-logic Studies Depression Scale	20 items / 10 / patient, inter-viewer, caregiver	To identify symptoms of depression;for screening purposes / 1 summated total score
Trunk Control Test	1 item / 2 / observer	Short simple measure of motor loss (sitting balance item) / 1 score
Motricity Index (leg)	3 items / 2 / observer	Short simple measure of motor loss (3 leg items) / 1 score
Position Sense Ankle	1 item / 2 / observer	To sense direction of passive ankle movement / 1 score
Star Cancellation Test	1 item / 5 / patient	Most sensitive single test for neglect / 1 score
Apraxia Test	15 items / 10 / observer	Using objects, imitation of gestures and actions / 1 summated total score
Glasgow Coma Scale	15 items / 5 / observer	Cutoff 8/15 to separate coma from non-coma / 1summated score with eye, motor and verbal subscores
COOP-WONCA	4 items/ 2 / caregiver	Measures physical fitness, mood, daily activities, health / 1 summated total score
Social Network Score	4 items/ 2/ caregiver, patient	Contacts with friends, participation in group activities, church membership / 1summated score

SDG: stroke-unit discharge guideline
2: Substantial indications: reliabiliy coefficients > 0.80 for the homogeneity (H), test-retest (TR), and interobserver (IO) agreement (if a scale contains few items a coefficient > 0.60 is also sufficient). When IO is assessed by Kappa, a coefficient > 0.60 is considered as substantial. The responsiveness (RS) of the scale is demonstrated by the ability to detect health changes in patients over time. The scale is able to differentiate (DIF) patient groups. Convergent (CON) validity is demonstrated by significant correlations between the scale scores and instruments measuring the same or closely associated domains.

Psychometric properties								Clinical feasibility /Remarks
Reliability		Clinical validity			Construct validity			
H	TR	IO	RS	DIF	CON	DIS	TS	
2	2	2	2	2	2	2	14	Most widely used ADL-scale
2	2	2	2	2	2	2	14	Brief, simple, most commonly used
0	2	2	2	2	2	0	10	One of the most commonly used brief mental tests
○	○	○	○	○	○	○	○	Simple to score; face validity seems to be good (same items as MMSE)
2	0	2	0	2	2	2	10	No influence of motor disturbances; good predictive validity; excellent screening instrument
NR	2	2	2	2	NR	NR	8	Very useful in routine clinical practice
2	2	2	2	2	NR	NR	10	Very useful in routine clinical practice
NR	2	2	0	2	0	0	6	Brief, simple
NR	2	2	0	2	○	○	6	Brief, simple, most sensitive single test for neglect
2	○	2	○	2	○	○	6	One of the few existing apraxia tests
NR	2	2	2	2	○	○	8	Simple; most widely used scale for level of consciousness
NR	2	1	1	1	2	2	9	Brief, simple, handy
○	○	○	○	○	○	○	○	Brief, simple

Discriminant (DIS) validity is shown by low correlations between the scale scores and instruments measuring different dimensions. TS means total score of the psychometric properties.
1: Moderate indications: data of study reviewed are not consistent, results are summarily presented, or the studies suffer from methodological flaws.
0: No clear indications: data do not support the criteria.
NR: Not relevant in view of the characteristic of the scale (theoretically one could score 2 points; if for example only one item exists homogeneity is perfect). Ellipses (○) indicate that there are no data available.
*: For clarity and brevity the table is presented without original data of the studies. Except for the new instruments all the instruments have been tested with actual strokes.

The Trunk Control Test (TCT)[10,29,30,31,32,33] and Motricity Index (MI)[10,29,30,32,33] have been developed for use after stroke. For predictive purposes in the SDG only the balance item of the TCT and the three leg items of the MI will be used. Their applicability in clinical practice is excellent.
The Position Sense of the affected Ankle Test[33] is important for balance and walking ability. It is part of the routine clinical examination and it is brief and simple to apply.
The Star Cancellation Test[10,11 ,34,35,36] is part of the Behavioural Inattention Test and it is the most sensitive single test for neglect; depending on the number of missed stars the seriousness of neglect can be measured.
The Apraxia Test[37,38] has recently been developed to assess (seriousness of) apraxia and it uses objects and imitations of gestures and actions.
The Glasgow Coma Scale[10,39,40] is the most widely used scale to assess level of consciousness.
The COOP-WONCA Charts instrument[15,41,42,43,44,45,46,47,48,49,50] has been selected to assess the strength of the caregiver. For this purpose the items about physical fitness, mood, daily activities and health will be used.

Table 3 presents our list of assessment instruments with cut-off points.

Table 3 SDG list of assessment instruments for prognostic factors

Premorbid situation	**Cut-off points**
1. Premorbid functional disability: premorbid Barthel Index	BI ≤ 18 out 20
2. Premorbid cognitive disability: Hetero Anamnesis Cognition	HAC ≥ 2 out 0-3
3. Premorbid depression and/or fear: premorbid CESD	CESD ≥ 16 out 60
Disease/Biology	
4. Severe stroke: lacunar/otherwise	Yes/no
5. Former stroke	Yes/no
6. Age of patient (≥ 70 years)	Yes/no
Body functions and structures	
7. Poor sitting balance: Modified Trunk Control Test	TCT yes/no
8. Severe hemiparesis/paralysis: Motricity Index affected leg	MI ≤ 27 out 100
9. Impairment in movement and position sense ankle affected leg	Yes/no
10. Neglect: Star Cancellation Test	SCT ≤ 50 out 54
11. Apraxia: Apraxia Test	AT ≤ 84 out 90
12. Depression and/or fear: CESD	CESD ≥ 16 out 60
13. Urinary incontinence: out of Barthel Index	BI ≤ 1 out 0/1/2
14. Loss of consciousness:Glasgow Coma Scale < 48 hours post-stroke	GCS ≤ 8 out 15
15. Personality disorder: DSM-IV code 310.1 by ICD9 code	Yes/no out 2
Activities	
16. Functional disability: Barthel Index	BI ≤ 6 out 20
17. Severe communicative disability: AAT level of communication	AAT ≤ 2 out 6
18. Severe cognitive disability: MMSE subsections language/memory/ attention/construction	MMSE ≤ 8 out 20
19. Disorientation in time and place: MMSE subsection orientation	MMSE ≤ 5 out 10
Family circle	
20. Supporting power partner: COOP-WONCA Charts	CO-WO ≥ 16 out
21. Readiness/availability family circle	Yes/no
22. Presence family circle: ≥ 4 x ½ hour a day	Yes/no
Social situation in general	
23. Availability professional care: ≥ 4 x ½ hour a day	Yes/no
24. Availability social network: social network score	SNS ≤1 out 0-4
25. Private financial means to buy care?	Yes/no
Residence	
26. House adapted to needs and abilities of the patient	Yes/no

SDG: Stroke-unit Discharge Guideline: scoring round day 7 - 10 post-stroke; **CESD**: Center for Epidemiologic Studies Depression Scale; Personality disorder as a result of an organic psychosyndrome; **DSM**[1]: Diagnostic Statistical Manual; **ICD**: International Classification of Diseases[2]; **AAT**: Aachen Aphasia Test; **MMSE**: Mini Mental Status Examination. The SDG scoring list, an explanation of the new instruments, and literature references of the known instruments can be downloaded via www.stichtingmyosotis.nl under AMDAS.

[1] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (4th ed. [DSM-IV]. Washington DC. 1994.

[2] World Health Organization. International classification of diseases. 9th rev. Clinical modification (ICD-9-CM). Geneva, Switzerland. 1978.

Discussion

For 17 of 26 factors from Table 2 we found known applicable assessment instruments, that fulfilled the criteria set beforehand. For two factors, namely premorbid cognitive disabilities and social network score, we had to construct a new instrument that will be subjected to further validity and reliability testing and is to be regarded as a proposition here. A simple clinical definition was used for the resulting seven factors.
As demonstrated in Table 2 the clinical feasibility of the instruments is good. The psychometric properties of most of the scales is sufficient to good; however, we should realise that the total possible score of fourteen will be not be reached by scales with NR scores (not relevant in view of the characteristic of the scale). Yet, the new scales will have to be validated.
A problem concerning sensitivity and specificity of the instruments could be that they have been established in diverse situations and populations. The instruments now will be applicated in the subacute stage of stroke at the hospital stroke-unit. This could affect their validity and almost certain their sensitivity and specificity and hence their predictive values. The cut-off points of the instruments have been chosen on the basis of scientific evidence, use in existing literature, and clinical experience. Indeed, ideally for every instrument a separate scientific study should be performed. Because of limitations in time and manpower this was impossible to achieve. So, the selection of the instruments and the chosen cut-off points has been done by semi-systematic searching. We could not find evidence that for the particular purpose of our research these instruments are necessarily the best in their own domain, or that the cut-offs are necessarily the best cut-offs.

USE OF THE SDG INSTRUMENTS IN CLINICAL PRACTICE AT THE STROKE-UNIT

Ideally the scoring should be done by the multidisciplinary treatment team, whereby each discipline scores the instruments of its own professional domain. Except for the apraxia test, MMSE, and CES-D, the scoring of the instruments is not time consuming.

The primary use of the SDG is for prognosis. But the scoring profile also is a handy instrument for evaluation of treatment effects, and evaluation of recovery, because many of the known SDG instruments are responsive to change. Another application is the use of assessments as a basis for choosing the rehabilitation goals and more specifically for formulating the specific therapy targets of the disciplines at the levels of functions, structures, and activities. Furthermore, the scoring of the assessment instruments in the subacute stage of stroke is of major importance for longitudinal data analysis. In our literature searches most articles from the rehabilitation setting had to be excluded, because patient selection was unclear and unexplained, without a clearly defined inception cohort, and because the first assessment of prognostic factors took place after the first two weeks post-stroke. With use of the SDG selection criteria now can be unambiguously specified, which forms a valid basis for research and generalization of prognostic and therapeutic results. The hospital stroke-unit is the first location to start with a uniform use of measurement instruments for stroke. In the (sub-)acute and in further stages of stroke in the transmural stroke-service chain other instruments should be added to get a longitudinal insight in the seriousness and recovery of the stroke in the diverse domains of disease, functions/structures, activities, and in future participation and autonomy.

In many of the investigated studies assessment instruments, such as the BI or the MMSE, were used that comprise more than one domain. For future studies we would advise the use of separate instruments or the

analysis of the individual domain scores to assess the prognostic qualities of each domain in order to make prediction as precise as possible. Mandatory for future research is a uniform and unambiguous definition of prognostic factors, such as personality disorder.
In our literature searches we did not find a conceptual framework that incorporated clinical as well as social factors. None of the studies contained all the prognostic factors of the SDG. This means that in these studies multicollinearity could be a problem, that is if one prognostic factor incorporates part of the effect of another factor or more other factors. For population based global prediction this does not need to be a problem, but for individual prognoses it is, because the validity and the precision of the prediction decrease.

FURTHER RESEARCH

In 2002 a multicentre prospective cohort study has been started in order to analyse the predictive qualities of the 26 prognostic factors for the decision of the discharge destination from the hospital stroke unit and for the residence at one year after stroke. After data-analysis the importance of the various factors, which are now only estimates, will be known and the optimal cutoffs can be determined. Finally we aim to construct an algorithmic decision model.
Future questions are: 1. Does our decision model contain all the relevant prognostic factors? The Delphi panel rejected some potential prognostic factors, like comorbidity and swallowing problems. These factors will be scored and analysed in separate studies. 2. Did we choose the best assessment instruments? The search for the best instruments has not yet been closed. Other instruments will be assessed and analysed separately. December 2003 the SDG assessment instruments have become part of the stroke service chain information system (CVA-KIS), recently developed professional and digital specifications for application in web

based electronic patient records nationwide[51]. This implies a very important step to further implementation.
The expected future results of the SDG are summarized in Table 4.

Table 4 Final goals, potential profit, relevance and impact of the guideline

Treatment and stroke care planning in the stroke service chains nationwide based upon scientific and clinical evidence
Minimisation of wrong discharge decisions
Optimal rehabilitation-/care route for the individual patient
Diminishing the misuse of hospital beds (cost reduction)
Optimal transparancy about medical decision making
Reduction of unwanted inter-professional variability
Documentation in size and number of capacity problems in the transmural stroke service chain based upon the matching of reliable and validated patient profiles with the inclusion criteria of the stroke service institutions
Establishment of a uniform and scientific basis for longitudinal data analysis in research

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Chapter 7

The stroke-unit discharge guideline, a prognostic framework for the discharge destination from the hospital stroke-unit A prospective cohort study

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Abstract

Objective: The purpose of our study was to investigate which factors during the subacute phase post-stroke have predictive value for the discharge outcome from the hospital stroke-unit.

Methods: In a prospective cohort of 338 patients admitted to a hospital stroke-unit 26 potentially prognostic factors, arranged in clinical and social sub-domains have been scored and analysed by binary logistic regression analysis. The outcome of the research consisted of the various discharge destinations.

Results: The overall predictive value of the discharge model is high (91%). Factors predictive of a poor discharge outcome are a low BI score (OR 0.78 per point increase; $p<0.001$), a poor sitting balance (OR 5.96; $p<0.001$), a depression (OR 7.23; $p<0.001$), post stroke cognitive disability (OR 3.51; $p=0.007$) and older age (OR 1.05 per point increase; $p=0.008$). If present a personality disorder, premorbid cognitive disability, as well as premorbid functional disability show a tendency to a poor discharge outcome, but these factors did not reach statistical significance in this study possibly due to their low prevalence. Readiness of the family circle to provide support was only significant in the univariate analysis.

Conclusions: Somatic, biological and psychological factors predict the discharge outcome. Functional and cognitive factors play a decisive role for the future ability to live independently after a stroke. The prognostic importance of social factors could not be demonstrated. Urine incontinence did not emerge as a prognostic factor. This is in contrast to scientific findings till now, but in accordance with clinical experience.

Introduction

The disadvantages of a wrong discharge destination from the hospital stroke-unit (nowadays 14%)[1] are huge: at societal level there is the misuse of hospital beds with extra costs, and at the level of the individual patient there is psychological suffering, a wrong rehabilitation program, time loss, and possibly a worse rehabilitation outcome.

Three factors are of main importance for the decision of the discharge destination: 1. the prognosis with regard to the situation of the patient six to twelve months post-stroke concerning his/her capabilities to live independently[2], 2. the prognosis to perform activities of daily life (ADL) and ambulation[3], and 3. the presence of social support[4]. Other factors are the therapeutic needs of the patient and patient preferences. Especially the prognosis for the final residence six to twelve months post stroke creates an important dichotomy in patients who will (eventually) return home versus those who will not. Home and old people's home in this definition mean living independently with or without support of the family circle or of professional carers. The crucial point regarding independently living is that the patient or the patient system is able to manage his/hers own affairs, including support of professional care.

However, the present research evidence base on predicting stroke unit discharge is incomplete and the scientific level of evidence is insufficient. This is not surprising, because apart from methodological flaws in the studies, none of the studies we examined described a conceptual framework as a basis for the choice of the prognostic factors that were examined in these studies. Until now, without a systematic view, the amount of investigated prognostic factors constitutes an amorphous mass for any unwary researcher. This also means that potentially significant factors have not been investigated. If research unintentionally ignores potential relevant prognostic factors, other collinear factors could wrongfully seem to be more significant as they

really are. Notably, the potential relevance of social prognostic factors has been disregarded, as well as the potentially prognostic adverse effects of premorbid disability.

With use of a "modified Delphi Technique"[5,6,7,8] the research findings of our systematic reviews[2,3,4] have been combined with clinical experience by expert opinions nationwide. This process yielded 26 prognostic factors, which have been arranged in a conceptual framework with clinical and social sub-domains. At present we are validating these 26 identified prognostic factors in a multicentre prospective cohort study. In this paper we present the first evaluation of this study, which measures the influence of these factors on the discharge outcome, consisting of the various discharge destinations, from the hospital stroke unit.

Methods

STUDY POPULATION

In 2003 over a four-month period 338 patients were admitted to three hospital stroke-units in different regions of the country. All stroke patients had been diagnosed by means of clinical examination and a CT-scan. The hospitals were part of a similar stroke service chain, in which also participated a rehabilitation centre stroke-unit, nursing homes with a stroke-unit and a long stay department, old people's homes, a district sick bay, home rehabilitation and care facilities, and general practitioners practices (see www.stichtingmyosotis.nl for the admission criteria of the institutions). In the hospitals the decision of the discharge destination from the hospital stroke-unit takes place in a multidisciplinary meeting around day seven to ten post-stroke. For the majority of the patients within one to two weeks a valid prognosis can be made, as was shown in the studies of our systematic reviews[2,3,4]. If a prognosis could not be made within this period, mostly because of serious complications such as a pneumonia, then the decision for discharge was postponed. Patients

who have recovered within seven days, or patients who suffered less impairments and disabilities will be discharged home earlier, if possible, but have been included in our study. Patients who died within the first days post-stroke have been excluded from our study.

REGULAR THERAPY AND (PARA-) MEDICAL INTERVENTIONS

At admission all patients got a CT-scan and regular medical diagnosis and treatment. As soon as the patients were medically stable they received a basic rehabilitation treatment on a one-to-one contact basis between therapist and patient. The rehabilitation teams consisted of the neurologist, the rehabilitation physician, a physiotherapist, an occupational therapist, a speech therapist, a nurse, a social worker, and a consultant psychologist. Once a week there was a multidisciplinary team meeting with regard to the therapy and progress of the patients, and to decide the destination of an eventual discharge.

OUTCOME

The outcome consists of the various discharge destinations from the hospital stroke-unit. The discharge destinations have been dichotomised into favourable discharge outcomes for patients who will return to an independent living situation (such as home, district sick bay, old people's home, rehabilitation centre and a limited stay in a nursing home stroke-unit department) versus poor discharge outcomes, that means not resulting in an independent living situation (nursing home long stay department, other hospital (department), and death before discharge). The final outcome of our prognostic study is the place of residence at one year. The current article describes the discharge destination from the hospital stroke unit as an intermediate outcome of the research. Independent living is defined as living at home or in an old people's home, with or without support of the family circle and/or professional care (the family circle consists of the spouse and/or other important persons who live together with the patient[4]). District sick bays or similar

institutions may serve as “hotel” facilities where the patient can recover from the stroke during a limited period of time and without receiving specific rehabilitation treatment. According to the admission criteria, from these institutions all patients will be discharged to an independent living situation. Admission to clinical rehabilitation in a rehabilitation centre is practically always followed by discharge to an independent living situation. Regarding a nursing home based stroke unit this percentage is about 75%. Therefore, discharge from hospital to a rehabilitation centre or to a nursing home based stroke unit is a favourable outcome. Transfer from a hospital stroke unit to another department in the hospital is regarded as a poor outcome, in case of serious complications with a poor prognosis for recovery.

PROGNOSTIC FACTORS

The potentially prognostic SDG factors have been arranged in seven clinical and social sub-domains encompassing 26 indicators. These indicators have been scored by use of assessment instruments (see Table 1). The assessment instruments have been chosen on the basis of three types of consideration: practical applicability, suitability for the stroke population, and psychometric qualities.

PROCEDURE

For all patients the scoring of the prognostic factors took place around day seven to ten post stroke. After admission on a regular basis (at least once a week) estimates were made in the multidisciplinary treatment team about improvements of every patient. As soon as possible the decision of the desired discharge destination was made and executed. The discharge destination from the hospital stroke-unit, being the outcome of the research of this article, was scored at time of discharge (see Figure 1).

Table 1 SDG list of assessment instruments for prognostic factors

Premorbid situation	**Cut-off points**
1. Premorbid functional disability: premorbid Barthel Index	BI ≤ 18 out 20
2. Premorbid cognitive disability: Hetero Anamnesis Cognition	HAC ≥ 2 out 0-3
3. Premorbid depression and/or fear: premorbid CESD	CESD ≥ 16 out 60
Disease/Biology	
4. Severe stroke: lacunar/otherwise	Yes/no
5. Former stroke	Yes/no
6. Age of patient (≥ 70 years)	Yes/no
Body functions and structures	
7. Poor sitting balance: Modified Trunk Control Test	TCT yes/no
8. Severe hemiparesis/paralysis: Motricity Index affected leg	MI ≤ 27 out 100
9. Impairment in movement and position sense ankle affected leg	Yes/no
10. Neglect: Star Cancellation Test	SCT ≤ 50 out 54
11. Apraxia: Apraxia Test	AT ≤ 84 out 90
12. Depression and/or fear: CESD	CESD ≥ 16 out 60
13. Urinary incontinence: out of Barthel Index	BI ≤ 1 out 0/1/2
14. Loss of consciousness:Glasgow Coma Scale < 48 hours post-stroke	GCS ≤ 8 out 15
15. Personality disorder: DSM-IV code 310.1 by ICD9 code	Yes/no out 2
Activities	
16. Functional disability: Barthel Index	BI ≤ 6 out 20
17. Severe communicative disability: AAT level of communication	AAT ≤ 2 out 6
18. Severe cognitive disability: MMSE subsections language/memory/ attention/construction	MMSE ≤ 8 out 20
19. Disorientation in time and place: MMSE subsection orientation	MMSE ≤ 5 out 10
Family circle	
20. Supporting power partner: COOP-WONCA Charts	CO-WO ≥ 16 out 2
21. Readiness/availability family circle	Yes/no
22. Presence family circle: ≥ 4 x ½ hour a day	Yes/no
Social situation in general	
23. Availability professional care: ≥ 4 x ½ hour a day	Yes/no
24. Availability social network: social network score	SNS ≤1 out 0-4
25. Private financial means to buy care?	Yes/no
Residence	
26. House adapted to needs and abilities of the patient	Yes/no

SDG: Stroke-unit Discharge Guideline: scoring round day 7 - 10 post-stroke; CESD: Center for Epidemiologic Studies Depression Scale; Personality disorder as a result of an organic psychosyndrome; DSM[1]: Diagnostic Statistical Manual; ICD: International Classification of Diseases[2]; AAT: Aachen Aphasia Test; MMSE: Mini Mental Status Examination. The SDG scoring list, an explanation of the new instruments, and literature references of the known instruments can be downloaded via www.stichtingmyosotis.nl under AMDAS.

[1] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (4th ed. [DSM-IV]. Washington DC. 1994.

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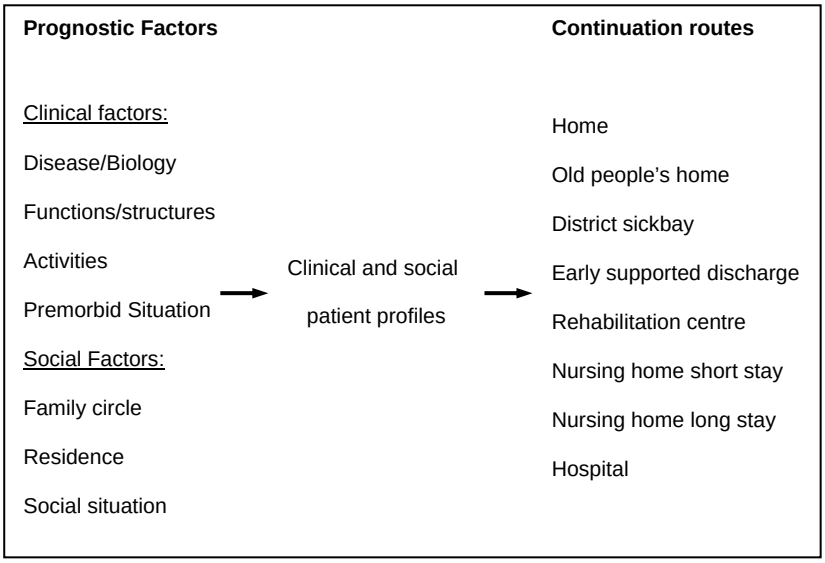

Figure 1: Stroke unit discharge model. The patient profile will be matched with the admission criteria of the continuation routes. Early supported discharge is not (yet) available in the Netherlands.

Every patient admitted was followed through the entire process; none dropped out of the study. It should be stressed that this research did not lead to any changes in the process and procedures of discharge decision making. Team decisions were made as usual. The only difference was that the scoring of the patients by the rehabilitation team was more complete and of higher quality than before the start of the research because of application of all SDG assessment instruments with best psychometric properties.

STATISTICAL ANALYSIS

Statistical analysis was conducted using Egret and SPSS10 statistical programmes. We applied binary logistic regression analysis using stepwise forward and backward selection procedures. Per sub-domain the

prognostic factors were put into the model as independent variables with favourable versus poor discharge destination as outcome. A model derived from a backward procedure had to be confirmed by a forward selection procedure before it was accepted. Effect ratios were expressed in odds ratios with 95% confidence intervals. Hosmer Lemeshow statistics were used to get an indication of the fit of the model. Nagelkerke R square statistics provided significance levels in formal testing of the fit of the model.

Results

PATIENT CHARACTERISTICS

Patient characteristics are presented in Table 2. No significant differences existed between study populations of the participating hospitals. Fifty percent of the admitted patients was over 70 years, 25% younger than 60 years, and 22% older than 80 years of age. The frequencies of severe stroke (42%) and recurrent stroke (24%) were high. Before the stroke a substantial number of patients showed functional disability (11%), cognitive disability (8%), or a depression (7%). In most cases the factors of the social sub-domain were favourable. Impairment in position and movement sense was the most frequently disturbed function (35%). Mortality of the total sample was limited to only 5.6% (19 patients), but together with 34 deceased from the first days post-stroke, who have been excluded from the research sample, the mortality percentage of all admitted patients became 16%.

Table 2 Patient characteristics measured from day 7 to 10 post-stroke

Items	**Scores in numbers**
Number of patients	338
Prognostic factors of the clinical sub domains	
- *Activities*	
Barthel Index mean/median (standard deviation)	12/14 (7)
Severe communicative disability	79
Cognitive disability	86
Disorientation in time and place	78
- *Premorbid situation*	
Premorbid functional disability	37
Premorbid cognitive disability	27
Premorbid depression and/or fear	22
- *Functions/structures*	
Poor sitting balance	97
Severe hemiparesis/hemiparalysis	94
Impairments in position and movement sense	118
Neglect	91
Apraxia	66
Depression and/or fear	44
Urine incontinence	113
Loss of consciousness (< 48 hours post-stroke)	11
Severe personality disorder	17
- *Disease/biology*	
Severe stroke (nature, localisation, size)	140
Former stroke	76
Age mean/median (standard deviation)	70/72 (13)
Dominant hemisphere	176
Ischaemic lesion	291
Sex (male : female)	176 : 162
Prognostic factors of the social subdomains	
- *Family circle*	
Abilities/sufficient supporting power	161
Readiness	193
Presence/availability	168
- *Social situation*	
Availability professional care	223
Presence social network	175
Personal financial means	44
- *Residence*	
Adapted to the needs and abilities of the patient	176
Outcome	
Home	143
District sick bay	1
Old people's home	9
Rehabilitation centre stroke-unit	35
Nursing home stroke-unit	60
Nursing home long stay department	66
Other hospital department	1
Deceased	19
Otherwise	4

MULTIVARIATE MODELLING

Multivariate modeling revealed that functional disability, poor sitting balance, depression, cognitive disability, and old age are significant predictors of a poor discharge outcome (see Table 3). The model corresponds to clinical experience, and it provides a logical prediction, in which one point increase of the BI (as instrument that measures functional disability) reduces the odds of a poor discharge outcome with 0.78. The presence of a poor sitting balance, a depression, a cognitive disability and an increase in age of one year enhance this odds with respectively 5.96, 7.23, 3.51 and 1.05. If present, personality disorder, premorbid cognitive disability, as well as premorbid functional disability show a tendency to a poor discharge outcome. However, possibly due to their low prevalence they did not reach statistical significance. Readiness of the family circle to provide support was only significant in the univariate analysis.

Table 3 Multivariate model to predict a poor discharge outcome

Variable	**B**	**SE**	**Sig**	**OR**	**95% CI for OR**	
					Lower	Upper
Barthel Index (Func Disab) (n)	-0.243	0.047	< 0.001	0.78	0.72	0.86
Poor sitting balance	1.784	0.484	< 0.001	5.96	2.31	15.38
Depression	1.979	0.584	< 0.001	7.23	2.30	22.73
Cognitive disability	1.256	0.464	0.007	3.51	1.42	8.79
Age (n)	0.051	0.019	0.008	1.05	1.01	1.09

1. B = coefficient of the factor; SE = standard error of B; Sig = significance; OR = odds ratio; CI = confidence interval; Func Disab = Functional Disability.
2. Functional disability has been scored by the Barthel Index, and higher scores on the Barthel Index reduce functional disability.
3. Functional disability and age have been scored on a numerical scale (n), poor sitting balance, depression and cognitive disability have been scored on a dichotomous scale.
4. Hosmer and Lemeshow Goodness of Fit: not significant; Nagelkerke R square: 0.74; overall predictive value: 91%; reciprocal correlation of the factors < 0.289; effect modification was absent.

Discussion

VARIABLES INCLUDED INTO THE MODEL

A major conclusion of our research is that significant prognostic factors for the in-hospital discharge outcome belong to the sub-domains of biology, functions, and activities, and notably not to the disease sub-domain. The results of our study are in line with former research findings[2,3]. Functional disability seems to be an important prognostic factor in all phases post stroke. Scored around day seven to ten it predicts for the level of activities of daily life and ambulation[9] and the future residence at six to twelve months after stroke[10,11,12,13]. Post stroke cognitive disability[10,12] as well as old age[12,14] worsen the odds to return to an independent living situation. Poor sitting balance seems to inhibit to reach independence in ADL[15]. Concerning post-stroke depression no studies with regard to prediction for discharge had been found[2,3].

VARIABLES EXCLUDED FROM THE MODEL

In accordance with scientific literature neither the side[15,16], nor the nature[15,16 ,17] of the lesion did show up as prognostic factors. It is remarkable that we could not demonstrate urinary incontinence as a predictor with regard to discharge outcome. This is in contrast to scientific literature[14]. Furthermore this incontinence is said to predict a worse functional outcome[9,14 ,18]. But urinary incontinence is a complex clinical phenomenon, and it probably is an indicator for a serious stroke[2]. In itself it is unlikely to be a reason why someone should not be able to live independently. Because of the relative completeness of the SDG with its large number of prognostic factors the model strongly reduces the likelihood of multicollinearity. This means that other factors, which are probably more important take over the predictive value of the factor urine incontinence.

Although in literature results about sex are contradictory[10,13,14 ,19,20] our study showed that sex, including interaction with age, had no prognostic influence. About social factors no data could be found in literature[4]. Of the social factors a readiness of the family circle showed a tendency to enlarge the odds of a favourable discharge outcome.

CONSIDERATIONS

The overall predictive value of the discharge model is high (91%). The emerged prognostic factors come from the sub-domains biology, functions, and activities and also contain the psychological factors cognitive disability and depression. Patients should be discharged to the optimal rehabilitation care route as soon as possible. Only then rehabilitation treatment will lead to the best results for the patient with the best cost-benefit ratio for society. For the majority of patients prediction around day seven to ten post-stroke is optimal[2,3,4]. A combination of the SDG with SSEP (somato-sensory evoked potentials) and MEP (motor evoked potentials) investigations could even yield more accurate predictions in specific cases, if these facilities are present[21,22,23]. However, for every patient we would advise to have a second moment for the prediction at one month post-stroke to evaluate, whether the chosen rehabilitation route is the right one. For almost all patients an optimal prediction of outcome can be made at one month post-stroke[24,25,26].

Patient views or preferences are no part of the SDG. The purpose of the SDG is to give an objective advice to the patient with regard to the best rehabilitation route. Subjective preferences should be no part of this advice. Finally, the patient and the physician will decide to the definitive choice on the basis of the objective advice and personal preferences.

The cut-off points of the instruments have been chosen on the basis of scientific evidence, use in existing literature, and clinical experience. Indeed, ideally for every instrument a separate scientific study should be

performed. Because of limitations in time and manpower this was impossible to achieve. So, the selection of the instruments and the chosen cut-off points has been done by semi-systematic searching. We could not find evidence that for the particular purpose of our research these instruments are necessarily the best in their own domain, or that the cut-offs are necessarily the best cut-offs.

Long-term studies are needed with a start of assessment at the hospital stroke-unit around day seven to ten post-stroke to obtain more reliable data on differences in prognostic factors during the sub acute phase after stroke and in the rehabilitation phase. We would advise the use of a conceptual framework, including clinical and social sub-domains[5].

Until now an evidence based discharge guideline for the decision of the discharge destination from the hospital stroke-unit is absent and these decisions have been made on the basis of clinical experience. Between hospitals differences in discharge policy do exist. Because health care systems differ between countries, in every country the patient profiles will have to be matched with the admission criteria of the available discharge institutions. To make this possible evidence based patient profiles will be needed.

The results of this study are only applicable for prediction around day 7-10 post-stroke. Prediction of the discharge outcome as short-term outcome is not necessarily synonymous with prediction of the optimal rehabilitation route and prediction of the optimal long-term outcome. As main final outcome of our longitudinal research in 2005 concerning 1000 patients the rehabilitation route and the residence at one year post-stroke will be compared to the predicted route and residence. After this last data analysis we expect to be able to construct an evidence based stroke-unit discharge guideline (SDG), by use of which patient profiles will be matched with profiles of the various discharge destinations.

Conclusions

The overall predictive value of the discharge model is high (91%). Our research into prognostic factors for the discharge outcome from the hospital stroke-unit is based upon a framework with clinical and social sub-domains, the SDG. The somatic factors functional disability and poor sitting balance, the biological factor old age, and the psychological factors cognitive disability and depression predict a poor discharge outcome.

So, functional and cognitive factors play a decisive role for the future ability to live independently after a stroke. The prognostic importance of social factors could not be demonstrated.

More research is needed regarding other potentially influential factors, such as comorbidity. Moreover, specific conditions like hemorrhage after acute ischemic stroke[27], stroke severity in atrial fibrillation[28], lacunar infarction[29], and results of laboratory investigations like MRI[29], and motor and somatosensory evoked potentials[30] should be investigated together with the factors of the SDG to improve and specify prediction.

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Clinical messages

- post-stroke functional and cognitive disabilities are important prognostic factors concerning discharge outcome

- further research is needed to the potential predictive value of social factors for the discharge outcome after a stroke
- improving and specifying individual prediction for discharge should be a target in stroke outcome research

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Chapter 8 

General discussion

Problems concerning prognostic research in stroke

The problems concerning the scientific base of prediction in stroke are manyfold, as was described in the introduction of this thesis. Until now the prognostic conceptual framework is weak, because of a deficiency of research into many potentially important prognostic factors, as well as an absence of a theoretical model, which incorporates these factors and categorises them into sub-domains. Moreover, the systematic application of the recommendations of the "Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap"[1] is insufficient, and as we have shown in our systematic reviews[2,3,4] , few studies sufficiently meet criteria of methodological quality. Many prognostic models for recovery after a stroke from all over the world have been examined, including many items like recovery of hand function, ambulation, ADL, and cognitive and communicative abilities. The number of models studied to predict the optimal discharge destination is less numerous. In the AMC Amsterdam a decision model for the discharge destination from the hospital stroke-unit was constructed in 1997 (table 1), but the predictive quality of this model proved to be insufficient. This is not surprising, because the factors are not evidence based, the assessment instruments (except for the BI and MMSE) are not valid and reliable, the weight of the factors is not valid, and judgements will be made on the basis of clinical experience.

WHAT SHOULD THEORETICALLY BE THE DEMANDS OF A STROKE-UNIT DISCHARGE GUIDELINE (SDG)

1. it should be based upon scientific and experimental evidence in accordance with the principles of evidence based practice.
2. it should consist of a conceptual framework of prognostic factors at the levels of disease, biology, functions, structures, and activities.

3. apart from clinical factors social prognostic factors also should be part of the framework, as well as premorbid factors.
4. the set of prognostic factors should be as complete as possible in order to eliminate multicollinearity, which means that one prognostic factor incorporates part of the effect of another factor or more other factors.
5. the assessment should be completed around day 7 to 10 post stroke, this being a clinically practicable and prognostically sound time point.

Table 1. Previous discharge decision model at the Stroke-unit AMC Amsterdam

Sc	Therapy	B.I.	Condition (x2)	Prognosis (x2)	Cognition (x2)	Homefront	Adaptation residence	Tot
3	None	16-20	Good	Complete recovery	Normal	Present Supporting power good	Not necessary	
2	Limited to 1 discipline	11-15	Moderate	Progress	Moderate disability	Partly present Supporting power moderate	Possible	
1	>1 discipline	6-10	Weak	Stable	Severe disability	Present Supporting power absent	Partly possible	
0	All disciplines	0-5	Poor	Deteriorate	Assessment not possible	Not present Supporting power absent	Not possible	

All factors have a scoring range from 0 through 3. The factors are: type and number of the therapies, level of ADL activities via Barthel Index, condition level, prognosis for recovery as measured by improvements during the therapies, cognitive situation via MMSE, presence and supporting power of the homefront, necessity and adaptability of the residence. Condition, prognosis for recovery and cognition have a double weight. Sc = score; B.I. = Barthel Index; Tot = Total score. Scoring range: 0-30.

A quick and well-considered choice of the discharge destination from a hospital stroke-unit is very important to realise the optimal rehabilitation route for the individual patient. Previous research in our centre showed that 14% of patients were discharged from the hospital to a non-optimal discharge destination[5], which to this day causes huge problems for the

patient and his family as well as at societal level. As we described in the introduction of this thesis, the trouble is that an evidence based discharge guideline was missing, and this was the motive to start our research. The objective of our research is the development of a guideline, the Stroke-unit Discharge Guideline (SDG), which aims to ensure an optimal discharge destination from the hospital stroke-unit. The basis of this guideline will be formed by scientific knowledge from systematic reviews into prognostic factors for functional recovery, and for the future residence after stroke, supplemented by expert clinical knowledge, taking into account the social circumstances of the patientT[6, 7, 8], which are also important in determining whether the patient can return home. Furthermore, we wanted to test the SDG in clinical practice by performing a multicentre prospective cohort study. As part of this thesis we have presented the results of a statistical analysis of the first 338 patients with respect to discharge destination as outcome variable.

How was the research performed? The SDG and Evidence Based Practice

We performed our systematic reviews (Chapters 2 through 4) in accordance with the Cochrane Collaboration criteria[9]. We used adequate binary outcome strategies as advised by the Evidence-Based Medicine Working Group[10], and in the presentation of our systematic reviews we applied the methods suggested by Moher et al.[11], which contain a checklist of standards that describes the preferred way to present the Abstract, Introduction, Methods, Results and Discussion sections of a meta-analysis or a systematic review, and which provide a flow diagram providing information about the number of studies identified, included, and excluded and a taxonomy of the reasons for excluding studies.

In our reviews all relevant publications were tested for internal, statistical, and external validity according to 11 methodological criteria[12] , which are in agreement with the general recommendations for studying prognosis in this field[13,14], and which have been recommended by the "Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap"[15] in order to improve the scientific quality and comparability of stroke outcome research. According to these criteria the publications were divided into three levels of evidence (A to C) , while we gave a higher value to internal and statistical items over external items of validity.

In a modified Delphi procedure the theses containing the prognostic factors were divided into four scientific levels, in accordance with the recommendations of the Stroke Guidelines 2000[16]. These levels depended on the number of A and/or B publications as basis for the prognostic factors in the theses.

To realise a high internal validity we performed our prospective multicentre cohort study by use of assessment instruments with best psychometric properties. At the start of our psychometrical research we determined the conditions the instruments should fulfill, whereby practical applicability at the hospital stroke-unit, suitability for the stroke population, and psychometric qualities[17] formed the main considerations. For most of the factors we could use known instruments, but for the factors "premorbid cognitive disabilities" and "presence of a social network", we had to construct new instruments, respectively the heteroanamnesis list cognition (HAC) and the social network score (SNS) (see further Hwww.stichtingmyosotis.nl). Before the start of the prognostic study we designed and tested adequate teaching and execution procedures for scoring and registration of the dependent and independent variables. One important result was that none of the patients dropped out of the studies .

The results of the studies: development of the SDG

The decision of the discharge destination from the hospital stroke-unit should be based upon the prognosis for the future living situation six to twelve months after a stroke, and for future functioning in ADL and ambulation, because ADL and ambulation capacities are of major importance for the ability to live independently. On the other hand the discharge destination should be in accordance with the current level of functioning of the patient, which means adapted to the bearing power of the patient, as well as capable of providing necessary care. Furthermore, the destination should be able to offer types and quality of treatment, which are considered to be essential in realising the rehabilitation goals, which the patient should be able to reach according to his/her wishes and the prognosis.

Accordingly we performed two systematic literature searches into potentially prognostic factors for the future living situation six to twelve months after a stroke, and for future functioning in ADL and ambulation. The presence of a clearly defined inception cohort with an assessment of prognostic factors within the first two weeks after stroke, and a follow-up duration of at least six months and a maximum of twelve months should be essential inclusion criteria.

After these searches had been carried out, an extra step was inserted because the searches did not yield any social prognostic factors. And this is in contrast to clinical experience because the presence of social support could be an important predictor of discharge destination[18,19]. Besides, in many cases the success of a return home is probably more affected by the characteristics of the primary caregiver, than by the characteristics of the stroke patients themselves[20]. So we performed a third systematic literature search into prognostic social factors during the subacute phase after a stroke for the discharge destination from the

hospital stroke-unit. As a result of our systematic literature searches the best evidence synthesis of level A studies leads to the following prognostic factors for a poor outcome:

- for ambulation and ADL **(Chapter 2)**: urinary incontinence, low initial Barthel Index, high age, severe paresis or paralysis, swallowing problems, ideomotor apraxia, ideational apraxia and visuospatial-construction problems; and as complications of an ischemic stroke: extraparenchymal bleeding, cerebral edema, and the size of intraparenchymal haemorrhage (more than moderate evidence existed for factors that have been supported by five level B studies, viz. unconsciousness/lowering of consciousness during the first 48 hours after stroke, tactile/visual inattention, and hemianopia).
- for independent living after six to twelve months **(Chapter 3)**: old age, female gender, non-lacunar stroke type, paresis of arm and leg, old hemiplegia, homonymous hemianopia, urinary incontinence, low initial ADL functioning, not alert as initial level of consciousness afther the stroke, visual extinction, constructional apraxia, visuospatial construction problems, low MMSE score, and no transfer to the stroke unit (supported by only some level B studies were the prognostic social factors marital status and a large social supportive network **(Chapter 4)**).

In all studies a conceptual framework as basis for the choice of the investigation of prognostic factors was absent. Especially, the presence of social prognostic factors was missing. The only factor with good scientific evidence for prognosis of ADL and ambulation, demonstrated by three level A studies, was urinary incontinence, but urinary incontinence is a complex clinical phenomenon and the underlying mechanism for its prognostic quality remains unclear. Probably, it

functions as indicator variable in case of a serious stroke. Apart from somatic disturbances cognitive disturbances seem to be of major importance for the ability to live independently. But in all respects insufficient scientific evidence exists for the clinical meaning of all the other identified prognostic factors, since no factor was demonstrated in at least two level A studies, our standard for scientific evidence.

To solve these problems we wanted to create a clear defined framework, based upon scientific and experimental evidence and consisting of prognostic factors at the levels of the premorbid physical and mental situation, disease/biology, functions/structures, and activities. Besides clinical prognostic factors social ones also should be part of the prognostic set. As mentioned in the introduction we performed a "modified Delphi Technique"[21] for this purpose, which procedure has the advantage of anonymously voting without face to face contact in the first postal rounds, combined with the possibility of discussion in the final consensus meeting, but in this meeting also with anonymous voting. As a novelty, for the postal rounds we used a digital procedure and especially for this procedure a website was developed, from where the panel members could answer the questions of the two digital Delphi rounds[22]. Out of 65 potential prognostic factors, from which eight had been presented by the panel members themselves, the final consensus meeting resulted in the construction of a conceptual framework, containing 26 prognostic factors arranged in four clinical and three social sub-domains **(Chapter 5)**. Once we had gathered the prognostic factors we had to look for assessment instruments to score them **(Chapter 6)**. The instruments should fulfill the following conditions: they should be suitable for prediction, practically to apply, suitable for the stroke population, and have good psychometric qualities.

For 17 out of the 26 prognostic factors we have found known applicable assessment instruments with sufficient to good clinical feasibility and

psychometric properties **(Chapter 6)**. For seven factors a simple definition was satisfactory. Because no suitable instruments that conformed with our conditions could be found to assess the premorbid cognitive disabilities and the presence of a social network, we constructed the heteroanamnesis list cognition (HAC) and the social network score (SNS) respectively for these factors. For all factors cut-off scores have been chosen on the basis of scientific evidence, supplemented by clinical experience.

For the factor "seriousness of stroke" a separate digital Delphi procedure was performed **(unpublished data)** with the participation of a panel of 12 expert neurologists nationwide and one expert physiatrist. The panel concluded that at the disease sub-domain for every stroke the nature (infarction versus haemorrhage, as diagnosed by CT-scan) and localisation (dominant versus non-dominant side, as diagnosed by clinical examination and/or CT-scan) should be recorded. Especially the nature of the stroke is of major importance in connection with thrombolysis as immediate therapy in the acute stage of stroke. With respect to prognosis the opinion was that the type of recovery between a haemorrhage and an infarction could be different, but not the final prognosis. Size of the lesion and old lesions should not be recorded routinely. The common opinion of the panel members was that factors of the activities and functions/structures sub-domains were by far the most inportant with respect to prognosis, in contrast to factors of the disease sub-domain. Nevertheless, scoring of the size of the lesion by the Bamford clinical classification of stroke[23] seems to be appropriate, because this score reflects the functional consequences of the anatomical lesion. Besides, research studies do exist that stress the potential importance of the size of the lesion[24,25].

As a next step, in conformance with national standards the guideline developer defined admission criteria for all types of discharge destinations. For the SDG we used the following levels[26]: 1. home; 2. district sick bay; 3. old people's home; 4. rehabilitation centre; 5. nursing home short; 6. nursing home long (> 6 months); 7. other hospital department; 8. death; 9.otherwise.

Now, having determined the assessment instruments, including cut-off scores, for measuring all prognostic factors, and having defined admission criteria for all discharge destinations the construction of the SDG was complete and the SDG was ready to be applied in patient care and in research.

The results of the studies: First Results of the Prospective Cohort Study

Multivariate modelling revealed that functional disability, poor sitting balance, depression, cognitive disability, and old age are significant predictors of a poor discharge outcome for the hospital stroke unit population. Premorbid cognitive disability, premorbid functional disability, and the presence of an organic psychosyndrome show a tendency to a poor discharge outcome. Possibly because of their small prevalence these factors did not reach statistical significance.
In accordance with scientific literature neither the side[27,28], nor the nature[27,28 ,29] of the lesion did show up as prognostic factors. Although in literature results about sex are contradictory[30,31,32,33,34], our study showed that sex, including interaction with age, had no prognostic influence. In contrast to scientific literature[32] we could not demonstrate urinary incontinence as a predictor with regard to discharge outcome.

The overall predictive value of the SDG discharge model turned out to be high (91%). To realise the best rehabilitation treatment for every patient we are of the opinion that patients should be discharged to the optimal rehabilitation care route as soon as possible. Only then rehabilitation treatment will lead to the best results for the patient with the best cost-benefit ratio for society. For the majority of patients prediction around day seven to ten post-stroke is optimal[2,3,4]. However, for every patient we would advise to have a second prediction at one month post-stroke to evaluate whether the chosen rehabilitation route is the right one. For almost all patients an optimal prediction of outcome can be made at one month post-stroke[35,36,37]. Long-term studies are needed starting the assessment at the hospital stroke-unit within two weeks post-stroke in order to obtain more reliable data on differences in prognostic factors during the subacte phase after stroke and in the rehabilitation phase. The SDG framework could be the basis for this[38,39].

Expected future results

The final goal of the SDG is a scientifically based choice for the discharge destination from the hospital stroke-unit with reduction of the chance for a wrong discharge destination, which nowadays is about 14%[40]. In relation to the incidence of 30.000 new stroke patients a year this is a major problem. Expected results of the introduction of the SDG will be realization of the *optimal rehabilitation-/care route* for the *individual patient, diminishing the misuse of hospital beds* (cost reduction) at the level of the organisations, and at societal level an optimal use of the limited means in health care. The *decision process* will become *more explicit* and will allow *more insight* into which factors are prognostically important; with which instruments they will be measured; how the factors in the situation of the individual patient will be weighed. This insight is *important for patients, relatives and doctors,* and makes

for a maximal clarity concerning the decision for the discharge destination. Due to a quick and reliable prediction concerning future abilities in daily life activities, ambulation and the possibility to live independently, the *patient and his relatives* can *prepare themselves for the future*, and they will be able *to communicate their preferences* as well**.** The transparency of the decision process will facilitate teaching medical trainees, it will *reduce unwanted inter-professional variability*, the process will become more accessible with respect to adaptation to new developments, and the transparency will enable testing medical practice. The College for Care Insurances, and the Ministry of Public Health, Welfare, and Sport in the Netherlands, who granted this research will get *optimal transparancy about medical decisions and lack of capacities in participating institutions*. Based upon the match of reliable and validated patient profiles with the admission criteria of the stroke care institutions *capacity problems* now can be *documented in size and number* for professionals and policymakers, who will receive reliable information for policy making. Because of the above-mentioned reasons it is to be expected, that the impact and the societal interest of the research will be substantial. Thanks to the well-defined clinical and social patient profiles the SDG should be an essential part of *benchmarking in the stroke service chain*. It provides regional data for capacity need of the various rehabilitation and care institutions.

Continuing research

When 1000 patient data will be available concerning the discharge destination from the hospital stroke-unit, the rehabilitation route and the residence one year post-stroke, the final data analysis of this part of the research will take place including regular statistical regression techniques

as well as by means of neural network analysis in favour of a digital advice system.
In conclusion, with the use of medical decision analysis techniques an algorithm will be constructed to support the decision process with respect to the discharge destination from the hospital stroke-unit. The expected result of future application of the SDG will be a more precise prediction leading to a reduction of the number of wrong discharge destinations with at least 30%, which equals a better discharge policy for over 1400 patients in the Netherlands each year.
The search for other potential influential factors has not yet been closed. As described in Chapter 5 the multidisciplinary Delphi panel of clinical stroke experts nationwide reached consensus about 26 out of 65 potential prognostic factors when deciding the discharge destination from a hospital stroke-unit. Some potentially prognostic influential factors, namely comorbidity and dysphagia, have been rejected by the Delphi panel. However, the correctness of their rejection may be debatable. For this reason, we are now studying these two factors seperately. The preliminary results of our **comorbidity study** suggest that pulmonary pathology predicts a worse discharge outcome, including mortality, although the association does not seem to be strong[41]. The comorbidity and dysphagia studies will be continued till sufficient patient data will be available for analysis of the results of their presumed predictive qualities. In the meantime validation and reliability studies are being carried out for the HAC (Hetero Anamnesis list Cognition) and the SNS (Social Network Score).

A next step in the SDG research will be the combination with laboratory investigations like MRI[42], motor and somatosensory evoked potentials[43], transcranial magnetic stimulation[44,45], etc. The ultimate goal will be a most precise prediction for the individual patient, meaning that future

prognostic research will be focused in an increasing degree on specific sub-populations of stroke such as haemorrhage after acute ischaemic stroke[46], stroke and atrial fibrillation[47], lacunar infarction[42], etc.
Another challenging subject, into which research has just started, will be the comparison of the SDG's prognostic qualities toward the NIHSS (National Institutes of Health Stroke Scale).
Cross-validation of the results of the various stroke-units is also a target. Not only will information be necessary about the clinical and social SDG patient data, about epidemiological data representing the specific regional sub-populations, but also information will be needed about logistic data representing type and number of regional institutions, including capacity data. Next, if these clinical patient data, epidemiological data and logistic data can be added to the current benchmarking items concerning the organisation of, the process of and satisfaction with the treatment, benchmarking will be founded upon complete information.

Furthermore, the scoring of the assessment instruments in the subacute stage of stroke is of major importance for longitudinal data analysis. The hospital stroke-unit is the first location to start with a uniform use of measurement instruments for stroke. In the (sub-)acute and in further stages of stroke in the transmural stroke-service chain other instruments can be added to get a longitudinal insight in the seriousness and recovery of the stroke in the diverse domains of disease, functions/structures, activities, and in future participation and autonomy.
The assessment goal will decide to what instruments should be used. For example, to predict recovery of hand function in the subacute stage of stroke the Motricity Index[48], the Fugl-Meyer Assessment Scale[49] and the Frenchay Arm Test[50] are only three possible instruments to use, which can be combined with laboratory investigations like evoked potentials[51].

The Amdas Project

After the development of the final version of the SDG we wanted to put it into a digital advice system for stroke. For this purpose the SDG project has closely cooperated with the Myosotis project. The Myosotis Digital Advice System for Stroke is a knowledge based digital information system that gives an advice about the optimal rehabilitation route in the subacute phase post stroke. The Corporation Myosotis has used the scientific data of the SDG as basis for the construction of this system. The name of the system is now called AMDAS (AMC Myosotis Digital Advice System for Stroke). By use of information and communication technology Myosotis' goal is to develop and implement instruments, that support the health care professional by providing data, information and knowledge. The next step was the integration of the AMDAS into a national electronic patient record for stroke, the CVA Chain Information System (CVA-KIS). Recently this CVA-KIS has been developed under the auspices of the National ICT Institute in the Care (NICTIZ)[52,53]. The electronic patient records will be equipped with functions that provide knowledge to the professional while he/she uses the record.

Dissemination and implementation

Due to its "neural net" type software, the AMDAS expert system is a dynamic and self learning system. This offers the opportunity for adaptation to new developments and to local situations. The SDG constitutes a uniform and scientific basis for longitudinal data analysis in stroke research, and is part of the CVA-KIS.

The CVA-KIS comprises numerous assessment instruments including the SDG instruments, and the NICTIZ panel members have come to an agreement about which instruments should be assessed at which location

and time point in the stroke-service chain[52]. For example, although a paresis of an arm is not a prognostic factor with regard to the future ability to live independently, of course the severity of the paresis of the arm has to be assessed by the Motricity Index just as a paresis of the leg. Another example could be the assessment of hypertonia of the muscles by application of the Ashworth scale[54]. So, clinimetric assessment will be used during the whole treatment process and also during the evaluation phase, and it certainly will not be restricted to prognostic purposes. The assessment goal will decide to what instruments should be used. The inclusion of the SDG instruments in the CVA-KIS provides an excellent vehicle for further dissemination and implementation of the SDG and the AMDAS. As stated before, the CVA-KIS and the AMDAS both easily can be adapted to new developments and research findings.

A growing number of stroke-units nationwide has started preparations to introduce the SDG.

However, expert education and instruction are required for a trouble-free introduction.

The region of Arnhem is the first region in the country where longitudinal data analysis is executed with a start of assessment at the hospital stroke-unit of Rijnstate Hospital and a continuation of the assessment with addition of new instruments at the stroke-unit of Groot Klimmendaal Rehabilitation Centre. A next step is the regional education and instruction with participation of the remaining regional hospitals, regional nursing homes and peripheral paramedical and home care institutions.

In our neighbouring countries colleagues have shown an interest to cooperate concerning the SDG subject.

Further implementation of the SDG and AMDAS will include 1. data-analysis of the first 1000 patients with respect to discharge destination and residence one year post stroke as main outcome variables by

multivariate regression techniques and neural network analysis, 2. construction of the SDG algorithm by use of medical decision making principles and techniques, 3. updating the AMDAS advice system, and 4. expert education and instruction to support a trouble-free introduction in the stroke-services nationwide.
The professional associations of the disciplines who participate in stroke care, the patient stroke organisation, NICTIZ, CBO, the College for Care Insurances, and the Ministry of Public Health, Wellfare and Sport will be involved in the further implementation of the SDG and AMDAS, so that finally the SDG will acquire broad acceptation nationwide and will be introduced nationwide in patient care as well as in benchmarking.

Stroke care worldwide and new developments

Health care and more specifically stroke care is changing and evolving worldwide.
Although integrated stroke care is now embedded in all stroke services in the world, the participating institutions differ. Dependent on the need for further rehabilitation therapy usually several treatment options are available, each with their own admission criteria. They consist of some form of inpatient or outpatient treatment in specialised care centres. In every country the SDG will have to be matched with the admission criteria of the available discharge institutions. The SDG provides a valuable clinical and social patient profile, that forms the basis for the prognosis and the therapy need of the patient. But also the SDG should evolve and should provide continuing steps for a more specific profile of the patient, enabling a more specific description of the therapy needs. This will demand application of more precise assessment instruments, which can be applied as a next step. For example, it is of paramount importance to identify the need for situation dependent and specific learning strategies in relation to the patient's possibility to improve in

activities of daily living (ADL) skills. It is well known that, the "learning context" and the context in which the acquired skills are to be used, should have essential characteristics in common[55,56]. Especially for patients with an impaired learning capacity the best learning situation to regain ADL independence, will be the real life situation at home. Where treatment at home is given or coordinated by a multidisciplinary team, Langhorne et al.[57] speak of early supported discharge (ESD). ESD could be a valuable alternative for a selected patient group and an adjunct to the available treatment options. Unfortunately, ESD does not (yet) exist in the Netherlands. From a clinical point of view, admission to ESD services will be the optimal choice for patients who no longer need medical and nursing treatment that only a hospital can provide; have moderate stroke severity; can return home because they can care for themselves or they have the help of professional care, family care, or both; need rehabilitation treatment that can be provided at home; do not need rehabilitation treatment that cannot be provided at home; live at a considerable distance from the hospital or rehabilitation services and for whom the combination of travelling to an outdoor service with exercise could be too tiring; or patients who would benefit most from situational learning instead of trying to generalise learned skills[58].

In conclusion: The SDG provides a clinical and social patient profile, that forms the basis for the prognosis and the therapy need of the patient. The SDG is applicable in every health care system and in every regional setting, but in every setting the SDG will have to be matched with the admission criteria of the available discharge facilities.

Appendix:

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a. Scoring list and explication of all SDG assessment instruments in Dutch and of the new instruments also in English
b. Literature references regarding the assessment instruments
c. Admission criteria of the institutions

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Summary

Samenvatting

Summary

INTRODUCTION (CHAPTER 1)

Every stroke patient should be transferred to a specialized stroke-unit , and medical and rehabilitative care should be organized in the form of a transmural stroke service chain. Next a quick and well-considered choice of the discharge destination is very important to realize the optimal rehabilitation route for the individual patient. The lack of evidence based criteria to formulate the discharge destination from the stroke unit is a problem, and uncertainty often exists about the correctness of the decisions taken. The CBO Stroke Guidelines 2000 do not contain a discharge guideline. Previous research in the AMC Amsterdam showed that 14% of patients were discharged from the hospital to a non-optimal discharge destination. An inappropriate discharge destination may cause a wrong rehabilitation program that decreases the chances of a favorable outcome, unnecessary psychological suffering for the patient and his/her family, potentially serious errors in long-term management, and inefficient use of health care facilities.

The problems concerning the scientific base of prediction in stroke are manifold. Until now the prognostic conceptual framework seems to be weak. For studies of prognosis the term inception cohort is used to describe a group of people who are assembled near the onset ("inception") of disease. The inception cohort of our research starts with suffering a stroke and being transferred to a hospital stroke-unit.

The objective of our research is the development of a guideline, the Stroke-unit Discharge Guideline (SDG), in order to realize an optimal discharge destination from the hospital stroke-unit.

Our research plan for developing the SDG consists of the following steps: systematic literature searches into prognostic clinical and social factors for the future living situation six to twelve months after a stroke,

for future functioning in ADL (activities of daily life) and ambulation, and for the discharge destination from the hospital stroke-unit. Next, a Delphi procedure with participation of a multidisciplinary panel of clinical experts representing the key disciplines of the transmural stroke service chain nationwide to design an evidence and experience based set of SDG prognostic factors, including assessment instruments, and scoring guidelines; definition of admission criteria of all discharge institutions in conformance with national standards. Subsequently, a multicenter prospective cohort study concerning the application of the SDG as a prognostic framework for the discharge destination from the hospital stroke-unit, including data-analysis with use of binary logistic regression analysis of the first 338 patients with respect to discharge destination as outcome variable.

Nowadays, evidence-based medicine has become an accepted basis for good clinical practice, and considerable efforts are made to implement it. The development of the SDG fits into this approach. We performed our prognostic research in accordance with the Cochrane Collaboration criteria, we used adequate binary outcome strategies as advised by the Evidence-Based Medicine Working Group, and in the presentation of our systematic reviews we applied the methods suggested by Moher et al.

SYSTEMATIC LITERATURE REVIEWS (CHAPTERS 2, 3 AND 4)

The objective of the reviews was to identify evidence based prognostic factors in the subacute phase after stroke for ADL and ambulation (Chapter 3), and for the future residence (Chapter 4) at six months to one year after stroke. These factors are of major importance for the discharge decision from the hospital stroke-unit. Because these two systematic reviews did not yield sufficient social prognostic factors, which is contradictory to our clinical experience, we performed a third sensitive systematic review to identify prognostic social factors in the subacute phase

after stroke for the discharge destination from the hospital stroke-unit (Chapter 5). The inclusion criteria for the studies were: 1) cohort studies of patients with an ischemic or haemorrhagic stroke; 2) inception cohort with assessment of prognostic factors within the first two weeks after stroke; 3) outcome measures for ADL and ambulation (Chapter 3), future residence (Chapter 4), discharge destination (Chapter 5); and 4) a follow-up of 6 months to 1 year. Internal, statistical and external validity of the studies were assessed using a checklist with 11 methodological criteria in accordance with the recommendations of the Cochrane Collaboration. The keywords used in the reviews are: prognosis, activities of daily living, ambulation, future residence, social situation, discharge destination, stroke-unit, systematic review.

Out of 1217 potentially relevant studies with respect to ADL and ambulation 26 studies involving a total of 7850 patients met the inclusion criteria, with respect to the future residence 10 studies involving a total of 3564 patients, and with respect to social factors for the discharge destination six studies involving a total of 929 patients.

With respect to ADL and ambulation incontinence for urine is the only prognostic factor identified in at least two level A studies (i.e. a good level of scientific evidence according to the methodological score). The following factors were found in one level A study: initial ADL disability and ambulation, old age, severe paresis or paralysis, impaired swallowing, ideomotor apraxia, ideational apraxia, and visuospatial construction problems; as well as factors relating to complications of an ischemic stroke, such as extraparenchymal bleeding, cerebral edema, and size of intraparenchymal hemorrhage.

With respect to the future residence no prognostic factor was identified in at least two level A studies. The following factors were found in at least one level A study: low initial ADL functioning, high age, cognitive disturbance, paresis of arm and leg, not alert as initial level of conscious-

ness, old hemiplegia, homonymous hemianopia, visual extinction, constructional apraxia, no transfer to the stroke unit, non-lacunar stroke type, visuospatial construction problems, urinary incontinence, and female gender.

With respect to the social situation marital status and social support proved to be important for prediction of the discharge destination. However, quantity and methodological quality of the research studies were insufficient, and the number of possible social prognostic factors investigated was limited by the absence of a conceptual framework of social sub-domains in the studies, including an unambiguous definition of the prognostic social factors within these sub-domains.

The conclusion of the reviews is, that the present evidence concerning possible predictors in the subacute stage of stroke has insufficient quality to make an evidence-based prediction of ADL and ambulation, and of the future residence after stroke. This is because only one prognostic factor was demonstrated in at least two level A studies, our cutoff for sufficient scientific evidence. The prognostic factors we identified belong to the domains of biology (e.g. age), disease (e.g. localisation of the lesion), functions (e.g. paresis) and activities (e.g. ADL). Furthermore, there is a need to use separate instruments to assess the prognostic qualities of the factors of each domain in order to make prediction as precise as possible, as well as to use a uniform and unambiguous definition of prognostic factors. We found that in the scientific research carried out until now social factors and their contribution to the possibility of living independently have not been investigated, or at least less well. None of the studies in our reviews described a conceptual framework as basis for the choice of the examined prognostic factors. Finally, we are of the opinion that a commitment about a conceptual framework of prognostic factors is mandatory.

A MODIFIED DELPHI PROCEDURE (CHAPTER 5)

Because scientific evidence, gathered from our systematic reviews, was insufficient and a conceptual framework was absent we wanted to extend the gathered prognostic factors with factors coming from expert opinions of a multidisciplinary team of clinical experts nationwide. The aim of this study was to reach consensus about the prognostic factors used when deciding the discharge destination from a hospital stroke-unit, and to construct a prognostic conceptual framework. To realise an optimal integration of knowledge from research findings and from opinions of experts in the field we used a "modified Delphi Technique", which is the most commonly used method for the production of clinical guidelines. This procedure yielded 26 prognostic factors, which were arranged in clinical and social sub-domains. The sub-domains and the factors within each sub-domain were prioritized according to their assumed predictive value for the decision process. The order of importance of the prognostic factors of the clinical domain was: 1. disabilities, 2. premorbid disabilities, 3. impairments, 4. disease/biology; and the order of importance of the factors of the social domain was: 1. homefront, 2. social situation, 3. residence. The Delphi procedure is an excellent instrument to determine and prioritize prognostic factors. With this procedure research-based and consensus-based knowledge can be combined. For a valid procedure it is mandatory to state explicitly in advance how the scores will be judged, and to explain the scientific level of the evidence during the whole procedure.

ASSESSMENT INSTRUMENTS (CHAPTER 6)

As part of our research to develop a consensus based guideline for the decision of the discharge destination from the hospital stroke unit, the SDG, the purpose of this paper is to present the design of an evidence based set of assessment instruments for the SDG prognostic factors. In

the literature of our systematic reviews and in known standard works we have looked for assessment instruments which are being used most frequently in stroke care, and subsequently we have searched for information regarding their validity and reliability. For 17 out of the 26 prognostic factors we found known applicable assessment instruments. Clinical feasibility and psychometric properties of most of these instruments are sufficient to good. For two factors we had to construct a new instrument. A simple definition was sufficient for the remaining seven factors. As a result the SDG contains an evidence based set of prognostic factors and assessment instruments, which should be applied at the hospital stroke-unit being the first location to start with a uniform use of assessment instruments after a stroke. The SDG assessment instruments are part of the CVA-KIS, recently by NICTIZ developed professional and digital specifications for application in national web based electronic patient records.

PROSPECTIVE COHORT STUDY (CHAPTER 7)

In this paper we present the results of the application of the SDG framework on the first 338 patients of a multicentre prospective cohort study. The outcome of the research consisted of the various discharge destinations. The binary logistic regression analysis shows an excellent overall predictive value of the discharge model (91%). Factors predictive of a poor discharge outcome are a low Barthel Index score (OR 0.78 per point increase; $p<0.001$), a poor sitting balance (OR 5.96; $p<0.001$), a depression (OR 7.23; $p<0.001$), post stroke cognitive disability (OR 3.51; $p=0.007$) and old age (OR 1.05 per point increase; $p=0.008$). If present a personality disorder, premorbid cognitive disability, as well as premorbid functional disability show a tendency to a poor discharge outcome, but these factors did not reach statistical significance in this study, possibly due to their low prevalence. Readiness of the family circle to provide support was only significant in the univariate analysis. Functional and

cognitive factors play a decisive role for the future ability to live independently after a stroke. The prognostic importance of social factors could not be demonstrated.

GENERAL DISCUSSION (CHAPTER 8)

The problems concerning the scientific base of prediction in stroke are manyfold, as we described in the introduction of this thesis. Until now the prognostic conceptual framework has been weak, because of a deficiency of research into many potentially important prognostic factors, as well as an absence of a theoretical model, which incorporates these factors and categorises them into sub-domains. Worldwide the number of models studied to predict the optimal discharge destination is scarce, and none of these models correspond to what we would call preliminary demands of a stroke-unit discharge guideline (SDG). The model of this guideline should be based upon scientific and experimental evidence in accordance with the principles of evidence based practice. It should consist of a conceptual framework of prognostic factors at the levels of disease, biology, functions, structures, and activities. Furthermore, clinical and also social prognostic factors should be part of the framework, as well as premorbid factors. The content of the framework should be as complete as possible to eliminate multicollinearity. This is the case if one prognostic factor incorporates a part of the effect of another factor or more other factors. The assessment should be completed around day 7 to 10 post stroke, being a clinically practicable and prognostically sound time point.

As stated in the introduction section we performed our prognostic research in accordance with the Cochrane Collaboration criteria, we used adequate binary outcome strategies as advised by the “Evidence-Based Medicine Working Group”, and in the presentation of our systematic reviews we applied the methods suggested by Moher et al. In our

systematic reviews we applied the recommendations of the "Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap", and during the Delphi procedure we applied the recommendations of the Dutch Stroke Guidelines 2000 with respect to the division of the prognostic factors into four scientific levels. Furthermore, in our own prospective multicentre cohort study we applied the same demands of internal, statistical and external validity criteria as we did to the studies of our systematic reviews, including the use of assessment instruments with best psychometric properties.

Development of the SDG was the first goal of our research. At first three systematic literature searches were performed. Next, factors presented by a multidisciplinary panel of clinical experts nationwide, representing all the key disciplines in stroke care were added to the prognostic factors yielded by these searches. Eventually, 26 prognostic factors, arranged in clinical and social sub-domains, were determined by the panel in a Delphi procedure. Subsequently assessment instruments with best psychometric properties for all factors were chosen. Finally, the admission criteria of all discharge destinations were defined. Now the construction of the SDG was complete and the SDG was ready to be applied in patient care and in research.

Multivariate modelling of the data from the prospective cohort study revealed that functional disability, poor sitting balance, depression, cognitive disability, and old age are significant predictors of a poor discharge outcome from the hospital stroke-unit. In accordance with scientific literature neither the side, nor the nature of the lesion did show up as prognostic factors. In contrast to scientific literature we could not demonstrate urinary incontinence as a predictor with regard to discharge outcome. But urinary incontinence is a complex clinical phenomenon, and it probably is an indicator variable for a serious stroke.

The overall predictive value of the SDG discharge model is high (91%). To realise the best rehabilitation treatment for every patient we are of the opinion that patients should be discharged to the optimal rehabilitation care route as soon as possible. Only then rehabilitation treatment will lead to the best results for the patient with the best cost-benefit ratio for society. For the majority of patients prediction around day seven to ten post-stroke is optimal. However, for every patient we would advise to have a second moment for the prediction at one month post-stroke to evaluate, whether the chosen rehabilitation route is the right one. For almost all patients an optimal prediction of outcome can be made at one month post-stroke.

The expected results of the introduction of the SDG will be realization of the optimal rehabilitation-/care route for the individual patient, diminishing the misuse of hospital beds, an optimal use of the limited means in health care, and a reduction of unwanted inter-professional variability. We will get optimal transparancy about medical decisions and about lack of capacities in participating institutions, so that capacity problems now can be documented in size and number. Because of the well-defined clinical and social patient profiles the SDG should be an essential part of benchmarking in the stroke service chain. The SDG constitutes a uniform and scientific basis for longitudinal data analysis in stroke research.

When 1000 SDG patient data will be available concerning the discharge destination from the hospital stroke-unit, the rehabilitation route and the residence at one year post-stroke, the final data analysis of this part of the research will take place including regular statistical regression techniques. The search for other potentially influential factors has not yet been closed. The comorbidity and dysphagia studies will be continued till sufficient patient data will be available for analysis of the results of their presumed predictive qualities. The first results of the comorbidity study

show that pulmonary pathology predicts a poor discharge outcome, including mortality, although the association does not seem to be strong. In the meanwhile validation and reliability studies are running for the HAC (Hetero Anamnesis list Cognition) and the SNS (Social Network Score). A next step in the research will be the combination of the SDG with laboratory investigations like MRI, motor and somatosensory evoked potentials, transcranial magnetic stimulation, etc. Another challenging research, which has just started, will be to compare the SDG's prognostic qualities toward the NIHSS (National Institutes of Health Stroke Scale). The SDG has been put into a digital advice system for stroke, the AMDAS. December 2003 the SDG assessment instruments have become part of the stroke service chain information system (CVA-KIS), recently developed professional specifications for application in web based electronic patient records nationwide. This CVA-KIS has been developed under the auspices of the National ICT Institute in the Care (NICTIZ).

The integration of the SDG instruments in the CVA-KIS provides an excellent vehicle for further dissemination and implementation of the SDG and the AMDAS. The CVA-KIS and the AMDAS both easily can be adapted to new developments and research findings.

Health care and more specifically stroke care is evolving worldwide. Although integrated stroke care is now embedded in all stroke services in the world, the participating institutions differ. For example, early supported discharge (ESD) services do not (yet) exist in the Netherlands. These services consist of treatment at home, which is given or coordinated by a multidisciplinary rehabilitation team.

In conclusion: The SDG provides a clinical and social patient profile, that forms the basis for the prognosis and the therapy need of the patient. The SDG is applicable in every health care system and in every regional set-

ting, but in every setting the SDG will have to be matched with the admission criteria of the available discharge facilities.

Samenvatting

INTRODUCTIE (HOOFDSTUK 1)

Iedere CVA patiënt dient te worden opgenomen op een gespecialiseerde stroke-unit en medische en revalidatiegeneeskundige behandeling dienen georganiseerd te zijn in een transmurale stroke service keten. Vervolgens is een snelle en weloverwogen keuze van de ontslagbestemming belangrijk om het optimale revalidatie traject voor de patiënt te realiseren. Het gebrek aan evidence based criteria om tot een goede ontslagbestemming vanuit de stroke-unit te komen is een probleem en vaak heerst er onzekerheid over de juistheid van de genomen beslissingen. De CBO Richtlijnen Stroke 2000 bevatten geen ontslag richtlijn. Een eerder in het AMC Amsterdam uitgevoerd onderzoek toonde aan dat 14% van de patienten naar een niet optimale ontslagbestemming vanuit het ziekenhuis werd ontslagen. Een verkeerde ontslagbestemming kan de oorzaak zijn van een verkeerd revalidatieprogramma waardoor de kans op een goede uitkomst afneemt, van onnodig psychisch lijden voor de patiënt en zijn/haar familie, van potentieel ernstige fouten in het lange termijn management en van inefficiënt gebruik van gezondheidszorgvoorzieningen. De problemen aangaande de wetenschappelijke basis van voorspellingen bij beroerte zijn talrijk. Tot op heden lijkt het prognostische conceptuele raamwerk zwak. Voor prognostische studies wordt de term inceptiecohort gebruikt om een groep mensen te beschrijven, die zijn samengevoegd bij het begin (“inceptie”) van ziekte. Het inceptiecohort van ons onderzoek begint met het krijgen van een beroerte en het worden opgenomen op de stroke-unit van een ziekenhuis.

Het doel van ons onderzoek is de ontwikkeling van een richtlijn, de Stroke-unit Discharge Guideline (SDG), met als doel het realiseren van een optimale ontslagbestemming vanuit de ziekenhuis stroke-unit.

Ons onderzoeksplan voor het ontwikkelen van de SDG bestaat uit de volgende stappen: een systematisch literatuuronderzoek naar prognostische klinische en sociale factoren voor de toekomstige woonsituatie zes tot twaalf maanden na een beroerte, voor het toekomstige niveau van functioneren wat betreft zelfredzaamheid en ambulantie, en voor de ontslagbestemming vanaf de ziekenhuis stroke-unit. Gevolgd door een Delphi procedure met deelname van een multidisciplinair panel van klinische experts die de sleuteldisciplines van de transmurale stroke service keten in het land vertegenwoordigen om een evidence en experienced based set van prognostische factoren samen te stellen, inclusief meetinstrumenten en richtlijnen voor het scoren ervan. Hierna komt een definitie van toelatingscriteria van alle ontslagbestemmingen in overeenstemming met nationale standaarden. Tot slot volgt een multicentrum prospectieve cohortstudie aangaande de toepassing van de SDG als prognostisch raamwerk voor de ontslagbestemming uit de ziekenhuis stroke-unit als uitkomstmaat, inclusief data analyse met gebruik van binaire logistische regressie van de eerste 338 patiënten.
In de huidige tijd is evidence based medicine geaccepteerd als uitgangspunt voor een goede klinische praktijkvoering, en veel energie is in de implementatie ervan gestoken. De ontwikkeling van de SDG past in deze benadering. We voerden ons prognostisch onderzoek uit in overeenstemming met de criteria van de Cochrane Collaboration, we gebruikten adequate binaire uitkomstmaten zoals geadviseerd door de Evidence-Based Medicine Working Group, en bij de presentatie van onze systematische reviews pasten we de methoden toe die zijn voorgesteld door Moher et al.

SYSTEMATISCHE LITERATUUR REVIEWS (HOOFDSTUKKEN 2, 3 AND 4)
Het doel van de reviews was om evidence based prognostische factoren te identificeren in de subacute fase na het CVA voor ADL (activiteiten

van het dagelijks leven) en ambulantie (Hoofdstuk 3), en voor de toekomstige woonsituatie (Hoofdstuk 4) zes maanden tot een jaar na het CVA. Deze factoren zijn van groot belang voor de ontslagbeslissing vanaf de ziekenhuis stroke-unit. Deze twee systematische reviews leverden onvoldoende sociale prognostische factoren op, hetgeen strijdig is met onze klinische ervaring. Daarom hebben we nog een derde sensitieve systematische review uitgevoerd om prognostische sociale factoren te identificeren in de subacute fase na het CVA voor de ontslagbestemming vanuit de ziekenhuis stroke-unit (Hoofdstuk 5). De inclusiecriteria voor de studies waren: 1) cohortstudies van patiënten met een ischemisch of haemorrhagisch CVA; 2) inceptiecohort met meten van de prognostische factoren binnen de eerste twee weken na het CVA; 3) uitkomstmaten voor ADL en ambulantie (Hoofdstuk 3), toekomstige woonsituatie (Hoofdstuk 4), ontslagbestemming (Hoofdstuk 5); en 4) een follow-up van 6 maanden tot 1 jaar. Interne, statistische en externe validiteit van de studies werden vastgesteld met gebruikmaking van een checklist bestaande uit 11 methodologische criteria overeenkomstig de aanbevelingen van de Cochrane Collaboration. De in de reviews gebruikte keywords zijn: prognose, activiteiten van het dagelijks leven, ambulantie, toekomstige woonsituatie, sociale situatie, ontslagbestemming, stroke-unit, systematische review. Van de 1217 potentieel relevante studies voldeden met betrekking tot ADL en ambulantie 26 studies met in totaal 7850 patiënten aan de inclusiecriteria, aangaande de toekomstige woonsituatie 10 studies met in totaal 3564 patiënten, en aangaande sociale factoren voor de ontslagbestemming 6 studies met een totaal van 929 patiënten. Met betrekking tot ADL en ambulantie is incontinentie voor urine de enige prognostische factor die is geïdentificeerd in tenminste twee niveau A studies (d.w.z. een goed niveau van wetenschappelijk bewijs overeenkomstig de methodologische score). De volgende factoren werden gevonden in een niveau A studie: initiële beperkingen in ADL en ambulan-

tie, hoge leeftijd, ernstige parese of paralyse, slikstoornis, ideomotore apraxie, ideationele apraxie en visuospatiële constructie problemen; eveneens factoren gerelateerd aan complicaties van een ischemisch CVA, zoals extraparenchymale bloeding, cerebraal oedeem en grootte van intraparenchymale bloeding. Ten aanzien van de toekomstige woonsituatie werd geen prognostische factor geïdentificeerd in tenminste twee niveau A studies. De volgende factoren werden gevonden in tenminste een niveau A studie: laag initieel niveau van ADL functioneren, hoge leeftijd, cognitieve beperkingen, parese van arm en been, initiële bewustzijnsdaling, oude hemiplegie, homonyme hemianopsie, visuele extinctie, constructieve apraxie, geen transfer naar de stroke-unit, niet-lacunair CVA type, visuospatiële constructiestoornissen, urine incontinentie, en vrouwelijk geslacht. Aangaande de sociale situatie bleken huwelijkse staat en sociale steun belangrijk te zijn voor het voorspellen van de ontslagbestemming. Echter, hoeveelheid en methodologische kwaliteit van de onderzoeksstudies waren onvoldoende en het aantal mogelijke sociale prognostische factoren dat was onderzocht was beperkt door de afwezigheid van een conceptueel raamwerk van sociale subdomeinen in de studies, waaronder een ondubbelzinnige definitie van de prognostische sociale factoren binnen deze subdomeinen.

De conclusies van de reviews zijn: in de eerste plaats, dat het huidige bewijs aangaande mogelijke predictoren in de subacute fase na het CVA onvoldoende kwaliteit heeft om een evidence-based voorspelling mogelijk te maken van ADL en ambulantie, en van de toekomstige woonsituatie na een CVA, omdat slechts één prognostische factor werd aangetoond in tenminste twee niveau A studies, ons afkappunt voor voldoende wetenschappelijk bewijs. Ten tweede, dat de prognostische factoren die we geïdentificeerd hebben behoren tot de domeinen van de biologie (b.v. leeftijd), ziekte (b.v. lokalisatie van de laesie), functies (b.v. verlamming) en activiteiten (b.v. ADL). Ten derde, dat er een behoefte bestaat om

aparte instrumenten te gebruiken voor het meten van de prognostische kwaliteiten van de factoren van elk domein teneinde de voorspelling zo precies mogelijk te maken, en tevens om een uniforme en ondubbelzinnige definitie te gebruiken van de prognostische factoren. Ten vierde, dat tot heden in het wetenschappelijk onderzoek sociale factoren en hun bijdrage aan de mogelijkheid om zelfstandig te wonen niet, of tenminste minder goed zijn onderzocht. Ten vijfde, dat geen van de studies in onze reviews een conceptueel raamwerk heeft beschreven als basis voor de keuze van de onderzochte prognostische factoren. En tenslotte, dat een bindende afspraak over een conceptueel raamwerk van prognostische factoren een vereiste is.

GEMODIFICEERDE DELPHI PROCEDURE (HOOFDSTUK 5)

Omdat het wetenschappelijk bewijs dat wij verkregen uit onze systematische reviews onvoldoende en een conceptueel raamwerk afwezig was wilden we de verkregen prognostische factoren uitbreiden met factoren afkomstig van meningen van een multidisciplinair team van klinische experts uit het hele land. Het doel van deze studie was om consensus te bereiken over de prognostische factoren die we gebruiken bij de beslissing over de ontslagbestemming uit de ziekenhuis stroke-unit, en om een prognostisch conceptueel raamwerk te construeren. Om een optimale integratie te bereiken van kennis afkomstig van onderzoeksbevindingen en van klinische ervaring van expert meningen gebruikten we een “gemodificeerde Delphi Techniek”, welke de meest gebruikte methode is voor de productie van klinische richtlijnen. De procedure leverde 26 prognostische factoren op, die werden gerangschikt in klinische en sociale subdomeinen. De subdomeinen en de factoren binnen elk subdomein werden geprioriteerd overeenkomstig hun veronderstelde voorspellende waarde voor het beslisproces. De volgorde van belangrijkheid van de prognostische factoren van het klinische domein was: 1. beperkingen, 2.

premorbide beperkingen, 3. stoornissen, 4. ziekte/biologie; en de volgorde van belangrijkheid van de factoren van het sociale domein was: 1. thuisfront, 2. sociale situatie, 3. woning. De Delphi procedure is een uitstekend instrument om prognostische factoren vast te stellen en te prioriteren. Met deze procedure kunnen onderzoeksgebaseerde en consensusgebaseerde kennis worden gecombineerd. Om een valide procedure te krijgen is het vereist om vooraf expliciet te verklaren hoe de scores zullen worden beoordeeld, en om het wetenschappelijk niveau van bewijs gedurende de gehele procedure toe te lichten.

MEETINSTRUMENTEN (HOOFDSTUK 6)

Als deel van ons onderzoek om een op consensus gebaseerde richtlijn, de SDG, te ontwikkelen voor de beslissing van de ontslagbestemming uit de ziekenhuis stroke-unit is het doel van deze studie om een ontwerp te presenteren van een op wetenschappelijk bewijs gebaseerde set van meetinstrumenten voor de prognostische factoren van de SDG. In de literatuur van onze systematische reviews en in bekende standaardwerken hebben we gezocht naar meetinstrumenten die het frequentst gebruikt worden bij de behandeling van CVA, en vervolgens zijn we op zoek gegaan naar informatie aangaande hun validiteit en betrouwbaarheid. Voor 17 van de 26 prognostische factoren hebben we toepasbare meetinstrumenten gevonden. Klinische toepasbaarheid en psychometrische eigenschappen van de meeste van deze instrumenten zijn voldoende tot goed. Voor twee factoren moesten we een nieuw instrument construeren. Een eenvoudige definitie volstond voor de overige zeven factoren. Als resultaat hiervan bevat de SDG een op wetenschappelijk bewijs gebaseerde set van prognostische factoren en meetinstrumenten. Deze kunnen worden toegepast op de ziekenhuis stroke-unit, die de aangewezen locatie is om te starten met een uniform gebruik van meetinstrumenten na een CVA. De SDG meetinstrumenten vormen een onderdeel van het CVA-KIS, recent door

het NICTIZ ontwikkelde professionele en digitale specificaties voor toepassing in nationale web based elektronische patiënten dossiers voor CVA.

PROSPECTIEVE COHORTSTUDIE (HOOFDSTUK 7)

In dit artikel presenteren we de resultaten van de eerste 338 patiënten van een multicentrum prospectieve cohortstudie betreffende de toepassing van de SDG als prognostisch raamwerk voor de ontslagbestemming vanaf de ziekenhuis stroke-unit. De uitkomst van het onderzoek bestond uit de verschillende ontslagbestemmingen. De binaire logistische regressie analyse toont een uitstekende voorspellende waarde van het ontslag model (91%). Factoren die een ongunstige ontslaguitkomst voorspellen waren een lage score op de Barthel Index (OR 0.78 per punt toename; $p<0.001$), een slechte zitbalans (OR 5.96; $p<0.001$), een depressie (OR 7.23; $p<0.001$), cognitieve beperkingen na de beroerte (OR 3.51; $p=0.007$) en hogere leeftijd (OR 1.05 per punt toename; $p=0.008$). Indien aanwezig toonden een persoonlijkheidsstoornis, premorbide cognitieve beperkingen, evenals premorbide functionele beperkingen een tendens tot een ongunstige ontslaguitkomst, maar deze factoren waren in deze studie niet statistisch significant, mogelijk vanwege hun lage prevalentie. Bereidheid van het thuisfront om steun te verlenen was alleen significant in de univariate analyse. Functionele en cognitieve factoren spelen een beslissende rol voor de toekomstige mogelijkheid om zelfstandig te wonen na een beroerte. Het prognostische belang van sociale factoren kon niet worden aangetoond.

ALGEMENE DISCUSSIE (HOOFDSTUK 8)

De problemen met betrekking tot de wetenschappelijke basis van predictie bij CVA zijn veelvuldig, zoals we in de introductie van dit proefschrift hebben beschreven. Tot op heden is het prognostische conceptuele

raamwerk zwak vanwege een gebrek aan onderzoek naar vele potentieel belangrijke prognostische factoren, evenals het ontbreken van een theoretisch model, dat deze factoren bevat en ze categoriseert in subdomeinen. Wereldwijd is het aantal modellen dat bestudeerd is om de optimale ontslagbestemming te voorspellen schaars, en geen van deze modellen komt tegemoet aan wat wij voorlopige eisen zouden willen noemen, die gesteld dienen te worden aan een stroke-unit ontslagrichtlijn (SDG). Het model van deze richtlijn behoort gebaseerd te zijn op wetenschappelijk en experimenteel bewijs overeenkomstig de principes van evidence based practice. Verder dient het opgebouwd te zijn uit een conceptueel raamwerk van prognostische factoren op de niveaus van ziekte, biologie, functies, structuren en activiteiten; behalve klinische behoren ook sociale prognostische factoren onderdeel te zijn van het raamwerk, evenals premorbide factoren. De inhoud van het raamwerk moet zo compleet mogelijk zijn om multicollineariteit uit te sluiten, d.w.z. dat een prognostische factor een deel van het effect van een andere of meer andere factoren bevat. En het meten moet worden uitgevoerd omstreeks dag 7 tot 10 na de beroerte, dat een klinisch praktisch en prognostisch juist tijdstip is.

Zoals in de introductie vermeld hebben we ons prognostisch onderzoek uitgevoerd overeenkomstig de criteria van de Cochrane Collaboration, en zijn door ons adequate binaire uitkomststrategieën gebruikt zoals geadviseerd door de “Evidence-Based Medicine Working Group”. Bovendien hebben we bij de presentatie van onze systematische reviews de methoden toegepast zoals voorgesteld door Moher et al. In onze systematische reviews zijn de aanbevelingen toegepast van de “Task Force on Stroke Outcome Research of Impairments, Disabilities and Handicap”, en gedurende de Delphi procedure zijn ten aanzien van de indeling van de prognostische factoren in vier wetenschappelijke niveaus de aanbevelingen toegepast van de Nederlandse richtlijnen Beroerte 2000. Verder trachten we in onze eigen prospectieve multicentrum cohort studie te voldoen aan

dezelfde eisen van interne, statistische en externe validiteit zoals we die hebben toegepast bij de beoordeling van de studies van onze systematische reviews, inclusief het gebruik van meetinstrumenten met de beste psychometrische eigenschappen.
De ontwikkeling van de SDG was het eerste doel van ons onderzoek. Ten eerste werden er drie systematische literatuur onderzoeken uitgevoerd. Vervolgens werden de in deze onderzoeken gevonden prognostische factoren aangevuld met factoren welke gepresenteerd werden door een multidisciplinair panel van klinische experts uit het hele land, die alle sleuteldisciplines in de behandeling van CVA vertegenwoordigden. In een Delphi procedure werden door het panel uiteindelijk 26 prognostische factoren vastgesteld, gerangschikt in klinische en sociale subdomeinen. Vervolgens werden voor alle factoren meetinstrumenten gekozen met de beste psychometrische eigenschappen. Tenslotte werden de toelatingscriteria van alle ontslagbestemmingen gedefinieerd. Hiermee was de constructie van de SDG voltooid en kon de SDG worden toegepast in patiëntenzorg en onderzoek.
Multivariate modellering van de gegevens uit de prospectieve cohortstudie toonde aan dat functionele beperkingen, een slechte zitbalans, depressie, cognitieve beperkingen en hoge leeftijd een ongunstige ontslaguitkomst voorspellen uit de ziekenhuis stroke-unit. In overeenstemming met de wetenschappelijke literatuur waren zowel in de ziekenhuis- als in de verpleeghuis- stroke-unit noch de zijde, noch de aard van de laesie van belang als prognostische factoren. In tegenstelling tot de wetenschappelijke literatuur konden we niet aantonen dat urine incontinentie een voorspeller was van de ontslaguitkomst. Maar urine incontinentie is een complex klinisch fenomeen, en waarschijnlijk is het een indicator variabele voor een ernstig CVA. De totale voorspellende waarde van het SDG ontslagmodel was hoog (91%). Om de beste revalidatie behandeling voor iedere patiënt te realiseren zijn wij van mening dat patiënten zo spoedig

mogelijk ontslagen dienen te worden naar het optimale revalidatie zorgtraject. Alleen dan zal revalidatiebehandeling leiden tot de beste resultaten voor de patiënt met de beste kosten-baten verhouding voor de maatschappij. Voor de meerderheid van de patiënten is voorspelling omstreeks dag zeven tot tien na het CVA optimaal. Echter voor iedere patient willen we een maand na het CVA een tweede moment voor voorspelling adviseren om te evalueren, of het gekozen revalidatietraject het juiste is. Voor bijna alle patiënten kan een maand na het CVA een optimale voorspelling gedaan worden met betrekking tot de uitkomst.
De verwachte resultaten van de toepassing van de SDG zijn: realisatie van het optimale revalidatie-/zorgtraject voor de individuele patiënt, een afname van het verkeerde gebruik van ziekenhuis bedden, een optimaal gebruik van de beperkte middelen in de gezondheidszorg en reductie van ongewenste interprofessionele variabiliteit. We zullen optimale transparantie verkrijgen aangaande medische beslissingen en betreffende een tekort aan capaciteit in de deelnemende instituten, zodat capaciteitsproblemen nu in maat en getal kunnen worden gedocumenteerd. Met zijn goed gedefinieerde klinische en sociale patiëntenprofielen behoort de SDG een essentieel onderdeel te zijn van benchmarking in de stroke service keten. De SDG vormt een uniforme en wetenschappelijke basis voor longitudinale analyse van gegevens bij CVA onderzoek.
Wanneer de SDG gegevens van 1000 patiënten beschikbaar zullen zijn betreffende de ontslagbestemming vanaf de ziekenhuis stroke-unit, het revalidatietraject en de woonsituatie een jaar na het CVA, kan de uiteindelijke analyse van de gegevens van dit deel van het onderzoek plaatsvinden. Hierbij zal gebruik gemaakt worden van reguliere statistische regressie methoden. De zoektocht naar andere potentieel invloedrijke factoren is nog niet afgelopen. De studies naar comorbiditeit en dysfagie zullen worden vervolgd totdat voldoende patiënten gegevens beschikbaar zullen zijn voor analyse van de resultaten aangaande hun vooronderstelde

voorspellende kwaliteiten. De eerste resultaten van de comorbiditeit studie tonen aan, dat longpathologie een voorspeller is van een ongunstige ontslaguitkomst, waaronder mortaliteit, hoewel de associatie niet sterk lijkt te zijn.
In de tussentijd zijn de validiteits- en betrouwbaarheidsstudies gaande naar de HAC (Hetero Anamnesis list Cognition) en de SNS (Social Network Score).
Een volgende stap in het onderzoek zal de combinatie zijn van de SDG met laboratorium onderzoeken zoals MRI, motore en somatosensore evoked potientials, transcraniële magneet stimulatie, enz. Een ander uitdagend onderzoek, dat zojuist is begonnen, is het vergelijken van de prognostische kwaliteiten van de SDG met die van de NIHSS (National Institutes of Health Stroke Scale).
De SDG is ingevoerd in een digitaal advies systeem voor CVA, het AMDAS. In december 2003 zijn de SDG meetinstrumenten onderdeel geworden van het CVA keten informatie systeem (CVA-KIS), recent ontwikkelde professionele specificaties voor toepassing in op het internet gebaseerde landelijke elektronische patiëntendossiers. Dit CVA-KIS is ontwikkeld onder auspiciën van het Nationaal ICT Instituut voor de Zorg (NICTIZ).
De integratie van de SDG instrumenten in het CVA-KIS verschaft een uitstekend middel voor verdere verspreiding en implementatie van de SDG en het AMDAS. Het CVA-KIS en het AMDAS kunnen beide gemakkelijk worden aangepast aan nieuwe ontwikkelingen en onderzoeksbevindingen.
De gezondheidszorg en in het bijzonder de zorg voor CVA is zich wereldwijd aan het ontwikkelen. Hoewel geïntegreerde zorg voor CVA nu in alle CVA ketens in de wereld is ingebed, verschillen de deelnemende instituten. Bijvoorbeeld vroeg ontslag met thuisbehandeling bestaat (nog)

niet in Nederland. Deze faciliteit bestaat uit behandeling thuis, die gegeven of gecoördineerd wordt door een multidisciplinair revalidatieteam. Tot slot: De SDG verschaft een klinisch en sociaal patiënten profiel, dat de basis vormt voor de prognose en behoefte aan behandeling van de patiënt. De SDG kan toegepast worden in elk gezondheidszorgsysteem en in elke regionale setting, maar in elke setting dient de SDG gematcht te worden met de instroom criteria van de beschikbare ontslagbestemmingen.

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Nabeschouwing

Tijdens mijn opleiding tot revalidatiearts in Revalidatiecentrum Heliomare in Wijk aan Zee in 1989 viel mij gedurende de stage op de CVA afdeling van mijn opleider Arie Prevo op, dat niet elke aanmelding voor klinische revalidatie vanuit het ziekenhuis voldeed aan de eisen, die passen bij een juiste indicatiestelling. Als jonge klare op mijn eigen CVA afdeling in de Sint Maartenskliniek in Nijmegen werd ik met ditzelfde fenomeen geconfronteerd. Op deze beide werkplekken heb ik vervolgens onderzocht hoe vaak patiënten met een CVA klinisch werden opgenomen met als doel om na de revalidatie naar een zelfstandige woonsituatie te gaan (al dan niet met ondersteuning) en hoe vaak deze doelstelling niet werd gerealiseerd. Frappant was, dat op beide plekken het percentage verkeerde verwijzingen 14% bedroeg. Vervolgens ben ik me gaan verdiepen in de criteria, die men op diverse plekken in het land hanteerde bij het kiezen van de ontslagbestemming vanuit het ziekenhuis. Meestal werd ingeschat of de patiënt na klinische revalidatie naar huis zou kunnen en of de thuissituatie daarbij zou kunnen ondersteunen. Frequent werd aangegeven, dat het praktisch lastig was om in een kort tijdsbestek een betrouwbare indruk te verkrijgen van de mogelijkheden van de patient en zijn systeem. Het meest opvallend was het ontbreken van een concept op grond waarvan de ontslagbestemming werd gekozen. Eenduidige criteria hiervoor ontbraken en de criteria die werden toegepast waren wetenschappelijk onvoldoende onderbouwd en onvolledig. Tijdens de VRA/SGO wetenschappelijke vormingscursus voor revalidatieartsen van 1996-1997 heb ik samen met mijn collega Bert Kriek voor dit probleem een onderzoeksvraag geformuleerd. Ten opzichte van de bestaande literatuur was het nieuwe van ons onderzoeksvoorstel, dat naast klinische factoren expliciet de sociale situatie van de patiënt als prognostische factor voor de ontslagbestemming werd bepaald. In deze periode waren mijn

ex-opleiders Guus Lankhorst en vooral Arie Prevo stand-by om vragen te beantwoorden en adviezen te geven. Maar in een gesprek met Arie Prevo en Eline Lindeman in november 1998 oordeelden zij, dat het door Bert Kriek en mij geformuleerde onderzoeksvoorstel veel te omvattend was om door mij te kunnen worden uitgevoerd naast een drukke baan als revalidatiearts-medisch manager in Medisch Centrum De Heel in Zaandam. Met Jacques van Limbeek met wie ik al vanaf 1995 over dit onderwerp brainstormde heb ik toen begin 1999 een beknopter onderzoeksvoorstel geschreven, dat ik tijdens mijn opleiding tot epidemioloog wilde uitvoeren en waarbij Jacques als arts-epidemioloog mijn stagebegeleider was. Inmiddels was in een tweetal promotieonderzoeken in het AMC naar de kwaliteit van de ziekenhuis zorg (Annemieke van Straten in 2000) en de lange termijn zorg na een CVA (Wilma Scholte op Reimer in 1999) geconstateerd, dat vanuit de ziekenhuis stroke-unit in het AMC Amsterdam ook 14% van de patiënten naar een suboptimale bestemming werd ontslagen. In gesprekken met Annemieke en Wilma werd het grote belang onderstreept van mijn onderzoeksvoorstel om een evidence based ontslagrichtlijn te ontwikkelen. Bij een inventarisatie in de regio Zaandam kwam ik weer op 14% uit. Dit betekende vermoedelijk twee dingen: 1. dat het probleem van een verkeerde ontslagbestemming in Nederland met grote waarschijnlijkheid in omstreeks 14% van de gevallen voorkomt, hetgeen 4200 patiënten per jaar betreft; en 2. dat gedurende een periode van 10 jaar, waarin de ziekenhuiszorg voor CVA patiënten geoptimaliseerd is door patiënten vanaf een algemene neurologieafdeling te concentreren op een stroke-unit, er geen verbetering in positieve zin heeft plaatsgevonden ten aanzien van het bieden van de optimale ontslagbestemming.

Vervolgens kwam ik in gesprek met Imelda de Groot, toenmalig afdelingshoofd van de revalidatieafdeling in het AMC. Zij zegde mij alle steun toe bij de opzet en uitvoering van een promotieonderzoek naar

prognostische factoren voor de ontslagbestemming vanaf de ziekenhuis stroke-unit. In een onderzoeksomgeving als in het AMC achtte zij het onderzoek door mij uitvoerbaar, hoewel ook zij het een veelomvattend onderzoek vond. Onder haar leiding werd subsidie aangevraagd bij het Centrum Richtlijnen Klinisch Handelen van het AMC en deze aanvraag werd gehonoreerd en overgenomen door het College voor Zorgverzekeringen. Aldus kon het onderzoek starten in november 1999, waarbij Daniela Ihnenfeldt, fysiotherapeute, bereid was om gedurende 1 jaar als medeonderzoeker te participeren. Begin 2000 kwam ik in gesprek met Hans van der Heijden, directeur van de Stichting Myosotis, welke stichting als doel heeft de informatievoorziening in de gezondheidszorg te optimaliseren. Myosotis had een digitaal adviessysteem voor CVA ontwikkeld met als input een beperkt aantal prognostische factoren. De stichting wilde graag gebruik maken van het prognostisch model, dat in mijn promotie onderzoek ontwikkeld zou worden. Als tegenprestatie mocht ik gebruik maken van de infrastructuur en ondersteuning van de stichting, die al in vele stroke-units in het land met de invoering van het adviessysteem bezig was met subsidie van het Ministerie van VWS. Met vol vertrouwen van beide partijen werd een joint venture gesloten om gezamenlijk een evidence based digitaal adviessysteem voor CVA te ontwikkelen, het AMC Myosotis Digital Advice System for Stroke (AMDAS), de neurale netwerk vorm van de Stroke-unit Discharge Guideline (SDG).

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Mijn tweede promotor prof. dr. R.J. de Haan, klinisch epidemioloog, beste Rob. Wat was ik blij toen jij bereid was te fungeren als mijn promotor, waarbij je op een rijdende trein moest stappen. “Clinimetrics in stroke” was jouw eigen promotie onderwerp destijds en dat heeft een aantal raakvlakken met het onderwerp van dit boekje. Naar aanleiding

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Curriculum vitae

Ronald Meijer was born on March 24 1948 in Amsterdam. From 1961 till 1966 he played football in the youth selection team of AFC Ajax Amsterdam and from 1965 till 1966 he was Dutch representative in UNESCO's Action International des Jeunes in Paris. In 1966 he graduated the gymnasium β, after which he had a working experience in a commercial bank for one year. In 1967 he started studying at the Academy for Physical Education in Amsterdam, which study he completed in 1971.
Starting as a draftee and later as a volunteer from 1971 till 1976 he was a NATO sports officer at various military bases in the Netherlands and in Germany.
After a two year advanced crash course in 1974 he achieved the certificate of football trainer grade 1 of the Royal Dutch Football Association. From 1972 till 1976 he was a trainer-coach at football clubs in the Netherlands and in Germany. After suffering a sports injury with heartache he decided to say goodbye to sport as a profession and only to exercise sports as a hobby.
From late 1976 through 1979 and from 1981 till 1985 he studied Medicine at the Free University in Amsterdam. After he graduated he worked as resident internal medicine, cardiology and rehabilitation medicine.
From 1987 till 1991 he followed post-graduate training at the Free University Amsterdam, Rehabilitation Center Heliomare Wijk aan Zee, Jan van Breemen Institute and Slotervaart Hospital both in Amsterdam.
From 1991 till 1997 he worked as a physiatrist in the Sint Maartenskliniek and in the University Hospital St. Radboud, both in Nijmegen . From 1996 through 1997 he followed the VRA/SGO scientific course.

As a member of the Rehabilitation Society of Hospitals in Noord-Holland from 1997 till end 1999 he worked as a physiatrist and as a medical manager at the rehabilitation department of Medical Center the Heel in Zaandam.
After a study of two years at the EMGO Institute of the Free University Amsterdam end 2000 he achieved his master of science in epidemiology.
From late 1999 through 2002 he worked as a physiatrist, epidemiologist, head of the medical service and acting representative instructor at the rehabilitation department of the Academic Medical Center Amsterdam.
End 1999 he started his dissertation research to the Stroke-unit Discharge Guideline.
From end 2002 till now he works as a physiatrist and epidemiologist at the Rehabilitation Center Groot Klimmendaal in Arnhem, where he also is acting representative instructor.

List of abbreviations

α (type 1) mistake	Just acceptable chance to detect an effect that is absent in reality (false positive)
β (type 2) mistake	Just acceptable chance to miss an effect that is present in reality (false negative)
1 - β = power of the research	Chance to detect a real effect
AAT	Aachen Aphasia Test
ADL	Activities of Daily Life
AMC	Academic Medical Centre
AMDAS	AMC Myosotis Digital Advice System for Stroke
ASB	Assessment of Cerebral Stroke and other Brain Damage
AT	Apraxia Test
B	Coefficient of the factor in a regression analysis
BI	Barthel Index
BIT	Behavioural Inattention Test
CES-D	Center for Epidemiologic Studies Depression Scale
CI	Confidence interval
CNS	Canadian Neurological Scale
COOP-WONCA	Charts to measure physical fitness, mood, daily activities and health of the caregiver
CT-scan	Computerised Tomography scan
CVA	Cerebral Vascular Accident
CVA-KIS	Stroke service chain information system
CVZ	College for Care Insurances
DSM	Diagnostic and Statistical Manual of Mental Disorders
Egret	A statistical program
ESD	Early Supported Discharge
FAI	Frenchay Activities Index
Family circle	People who live in the same home as the patient
GCS	Glasgow Coma Scale
HAC	Hetero Anamnesis list Cognition
IADL	Instrumental ADL items

ICD	International Classification of Diseases
ICF	International Classification of Functions
ICIDH	International Classification of Impairments, Disabilities and Handicaps
ICT	Information and Computerized Technology
Inception cohort	Group of people formed at the start of an event
IVZ	Corporation for information facilities in health care
MEP	Motor evoked potentials
MI	Motricity Index
MMAS	Modified Motor Assessment Scale
MMSE	Mini Mental Status Examination
Modified Delphi Technique	Most commonly used method for the production of clinical guidelines
MRI	Magnetic Resonance Imaging
Multivariate modelling	Statistical method using regression techniques
Myosotis	Corporation for information facilities in health care
N	Number of subjects
NICTIZ	National ICT Institute in the Care
NIHSS	National Institute of Health Stroke Scale
OR	Odds Ratio
p	Probability
Premorbid	Before the start of a disease
Prevalence	Frequency of occurrence at a certain moment or during a certain period
Psychometrics	Statistical characteristics of measurement instruments
SCT	Star Cancellation Test
r	Correlation coefficient
SD	Standard deviation
SDG	Stroke-unit Discharge Guideline
SE	Standard error
SMES	Sødring Motor Evaluation of Stroke Patients
SNS	Social Network Score
Social situation	Encompasses personal financial means, availability in the society of professional care, and quality of the social network of the patient
SPSS	Statistical Products and Service Solutions

SR	Systematic review
SSEP	Somato-sensory evoked potentials
SSS	Scandinavian Neurological Stroke Scale
TCT	Trunk Control Test
TIA	Transient ischemic attack
VWS	Ministry for General Health, Welfare and Sport
WHO	World Health Organization