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General introduction

THE GLOBAL BURDEN OF STROKE

According to the World Health Organization (WHO), stroke is defined as “rapidly developing clinical symptoms and/or signs of focal, and at times global, loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.”¹ Worldwide, 16.9 million people experience a stroke each year,² with 5.9 million of them dying² and another 5 million remaining permanently disabled.³ With a prevalence of 33 million,² stroke is the second cause of mortality⁴ and third cause of disease burden (expressed as ‘disability-adjusted life years’; DALYs).⁵ However, the trend for the age standardized-incidence of stroke is diverse for different parts of the world.² In low to middle income countries the incidence rate increases, while in high-income countries a significant decrease is perceived.⁶ Nevertheless, the prevalence of stroke remains high and even increases, due to the ageing population.^{2,3} When looking at the economic burden, the costs for stroke amounted to \$ 38.6 billion in the United States in 2009⁷ and these costs will substantially increase in the next few decades with a 129%.⁸

CLASSIFYING THE EFFECTS OF STROKE

The clinical presentation⁹ and etiology¹⁰ of stroke are diverse.¹¹ The wide spectrum of the clinical manifestations can be classified according to the International Classification of Functioning, disability and health (ICF).¹² This generic ICF-framework was developed to describe and measure health and disability, by subdividing health-related domains into body functions and structures, activity and participation, personal factors, and environmental factors (see Box 1.1).¹³ In addition, condition-specific ICF Core Sets were developed for a dozen burdensome chronic conditions including stroke,¹⁴ based on preliminary studies and formal consensus processes. These ICF Core Sets aimed to describe the wide range of problems that patients with that specific condition experience. The extent of the Comprehensive ICF Core Set for stroke, including 130 ICF-categories, reflects the wide variety of domains that are affected by stroke.¹⁴ As can be seen from Figure 1.1, the most common limitations in poststroke function(ing) comprise for example mental functions, attention functions, muscle power functions, and walking and other basic activities of daily living (ADL) like toileting and eating.¹⁴ Likewise, stroke-related consequences interact with environmental factors like immediate family and the patient’s need for health care services and professionals.¹⁴

To reduce the effects of stroke, the majority of patients enter a rehabilitation trajectory. For most of them, the final goal of stroke rehabilitation is to live independently at home¹⁵ and being integrated in community life. However, an estimated 25% to 74% of the stroke survivors require some assistance

Box 1.1 Definitions of the International Classification of Functioning, disability and health (ICF) in the context of health¹²

Functioning is an umbrella term for body functions, body structures, activities and participation. It denotes the positive aspects of the interaction between an individual (with a health condition) and that individual's contextual factors (environmental and personal factors).

Disability is an umbrella term for impairments, activity limitations and participation restrictions. It denotes the negative aspects of the interaction between an individual (with a health condition) and that individual's contextual factors (environmental and personal factors).

Body functions – The physiological functions of body systems (including psychological functions).

Body structures – Anatomical parts of the body such as organs, limbs and their components.

Impairments – Problems in body function and structure such as significant deviation or loss.

Activity – The execution of a task or action by an individual.

Participation – Involvement in a life situation.

Activity limitations – Difficulties an individual may have in executing activities.

Participation restrictions – Problems an individual may experience in involvement in life situations.

Environmental factors – The physical, social and attitudinal environment in which people live and conduct their lives. These are either barriers to or facilitators of the person's functioning.

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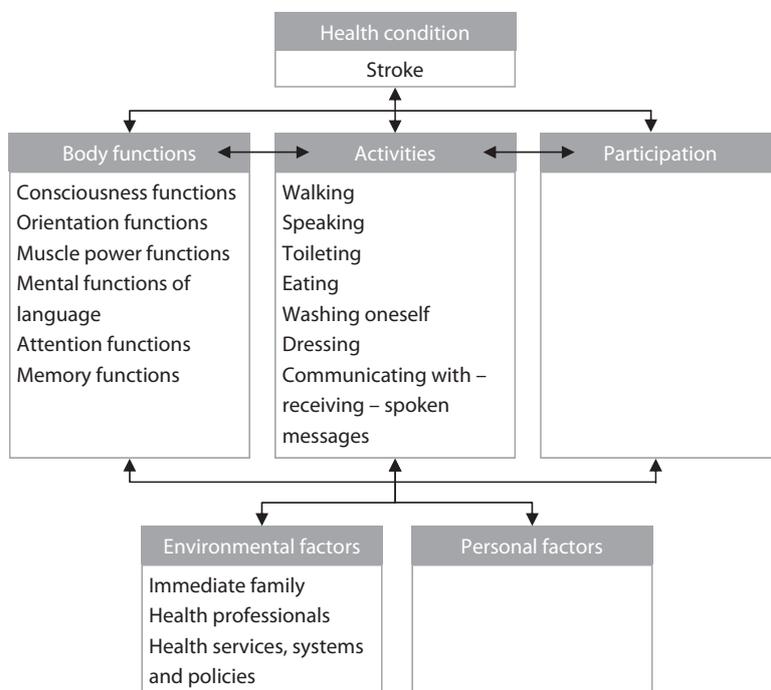


Figure 1.1 Brief ICF Core Set for stroke¹⁴

or are fully dependent on family caregivers for performing ADL.¹⁶ About 80% of the patients reach their best functioning in basic ADL within 6 weeks after stroke, and 95% within 12.5 weeks.¹⁷ Almost the same applies to walking which is closely related to ADL; 95% of the patients reach their plateau in walking performance 11 weeks after onset¹⁸ and 60%^{18,19} to 80%^{20,21} regain independent ambulation. These two rehabilitation outcomes, but also for example upper limb functioning,²² show a similar recovery pattern, displaying the most improvement within in the first 3 to 4 weeks poststroke which levels off with the passing of time and plateaus at 3 to 6 months poststroke.^{23,24}

Poststroke recovery is a complex process, and the mechanisms which drive these improvements poststroke are still under debate.²⁵ However, both restitution in terms of spontaneous neurological processes (e.g. resolution of diaschisis, restitution of penumbral areas, tissue repair) and substitution as a learning-dependent process (i.e. behavioral compensation) are thought to contribute to improvements within 6 months after onset.^{23,25}

STROKE CARE AND COMPLEX REHABILITATION INTERVENTIONS

After stroke onset, the vast majority of the patients is admitted to a hospital stroke unit, which provides specialized stroke management by an interdisciplinary team.²⁶ It has been shown that patients with stroke benefit from this type of organized care when compared to other forms of care. Their odds for survival, independency in ADL, and living at home one year poststroke are significant higher and are found to be independent of age, sex, severity, or type of stroke.²⁶

The first hours after stroke, the so called hyper acute phase, are focused on medical diagnostics, prevention of death, and if indicated, application of medical interventions like recombinant Tissue Plasminogen Activator (rTPA) in ischemic stroke.^{27,28} Being one of the cornerstones of poststroke care when the patient is medically stable, rehabilitation is initiated as soon as possible to facilitate functional recovery poststroke.²⁵ Stroke rehabilitation consists of a complex package of interventions applied by a team of health care professionals who collaborate intensively,^{26,29-31} and is assumed to be an important component of effective stroke care.³² According to the Medical Research Council, "Complex interventions are usually described as interventions that contain several interacting components. There are, however, several dimensions of complexity: it may be to do with the range of possible outcomes, or their variability in the target population, rather than with the number of elements in the intervention package itself."³² Based on their complexity, rehabilitation interventions can be divided in three levels: the service level, the operator level, and the treatment level (see Box 1.2).²⁹

Box 1.2 Rehabilitation interventions, classified according to levels of complexity²⁹

Service level	Interventions typically provided by more than one individual, each providing a complex package of care in a specific context and interacting with others in a complex way (e.g. stroke units, early supported discharge services)
Operator level	Interventions typically provided by a single operator such as the therapist or nurse, who provides a complex package of care that could incorporate both the personal interaction between the therapist and patient plus the therapy they provide (e.g. physical therapy in the patient's home environment, stroke family support workers)
Treatment level	Evaluation of the impact of a specific individual treatment (e.g. speed dependent treadmill training, constraint-induced movement therapy)

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Although rehabilitation is typically initiated at the hospital stroke unit, it is often continued after discharge as long as there are rehabilitation goals. The main goal of stroke rehabilitation is to reduce an individual's disability and handicap as a result of stroke by going through a cyclic process.²⁵ This cyclic process consists of (1) the assessment of the patient's needs; (2) realistic goal setting, taking into account the functional prognosis; (3) the selection and application of relevant intervention(s); (4) reassessment to monitor the clinical course, progress, and stated goals; and finally (5) completion of the treatment.^{25,33}

Physical therapy is one of the key disciplines in interdisciplinary stroke rehabilitation and present in the whole continuum of stroke care. Physical therapists have the expertise to assess and treat movement disorders and mobility limitations, aiming to reduce impairments and limitations in activities and participation throughout the lifespan.^{34,35} In addition, they play an important role in predicting functional outcomes poststroke in terms of walking ability, arm-hand activities, and ADL.²⁴

EARLY PROGNOSIS OF AMBULATION AND BASIC ADL POSTSTROKE

Although inspection of the recovery pattern of individual patients with stroke shows heterogeneity, there are indications that it is possible to make a first prognosis of functional outcomes within the first weeks poststroke.^{23,24} Predicting functional outcome after stroke is necessary for the interdisciplinary team to ascertain an appropriate rehabilitation trajectory, including the selection of a discharge destination; defining realistic rehabilitation goals with corresponding interventions; and inform the patient and caregivers. Prognostic models can be defined as "models that use

multiple prognostic factors in combination to predict the risk of future clinical outcomes in individual patients.³⁶ Based on prognostic studies, it appears that among other things age,³⁷⁻⁴⁰ impairment of sensory and motor function of the paretic leg,^{18,38,41} homonymous hemianopsia,^{38,41} sitting and standing balance,^{40,42} and initial disability in ambulation and ADL^{18,38,40} are determinants for ambulation abilities at 6 months poststroke. These determinants largely correspond with predictors for basic ADL.^{39,43-46} However, most of these variables independently associated with outcome in terms of ambulation and/or ADL were measured 7³⁹ to 14 days^{40,41} poststroke. The decreasing length of hospital stay over the last decades⁴⁷⁻⁴⁹ from 10.2 days in 1989 to 5.3 days in 2009⁴⁸ in the United States, requires bringing forward the timing of making this functional prognosis after stroke. Therefore, the ability of determinants to accurately predict outcomes after stroke, measured earlier than these above reported 7 to 14 days, to accurately predict outcomes after stroke should be established.

An overview of early measured variables able to predict or, contrary, not predict outcome in terms of basic ADL at least 3 months poststroke is given in **chapter 2**. For this purpose, a checklist was developed to assess the methodological quality (i.e. risk of bias) of publications reporting on prognostic studies. Based on the risk of bias and the identified variables, a best-evidence synthesis was performed to weight the evidence for each predictive and nonpredictive variable.

The Barthel Index (BI)⁵⁰⁻⁵² assesses the patient's actual performance of basic ADL, like washing oneself, eating, and transportation. This measurement is frequently used in hospital stroke units. In **chapter 3**, the predictive value of the BI measured within 72 hours after onset for outcome in basic ADL 6 months poststroke was investigated, based on data of a cohort consisting of first-ever ischemic stroke patients admitted to a hospital stroke unit. Subsequently, the earliest, most optimal, moment of assessment within 2 weeks after onset to accurately predict basic ADL was determined.

In **chapter 4**, a prediction model for outcome of independent gait 6 months after stroke is presented. The purpose of the study was to investigate whether independent gait could be predicted within 72 hours poststroke using a set of easily measurable clinical variables. In addition, the accuracy of this prediction model was investigated by reassessing these variables at days 5 and 9 after onset.

A NATIONAL CLINICAL GUIDELINE FOR PHYSICAL THERAPY POSTSTROKE

Clinical guidelines are developed in pursuit of high quality, uniform, and transparent care and are valued an important tool “to achieve effective health care.”^{53,54} In combination with clinical experience and the patient’s preferences, this available best-evidence should be incorporated in clinical reasoning and the treatment of the individual patient (i.e. evidence-based practice⁵⁵).

As for stroke rehabilitation, it has been shown that adherence to stroke rehabilitation guidelines improves patients’ outcomes in terms of performance of ADL, quality of life, discharge to home, and also satisfaction.⁵⁶⁻⁶⁰ The surplus value even increased when the interdisciplinary team had a higher compliance to these guidelines.⁶⁰

As mentioned previously, poststroke care has a strong interdisciplinary character and in the Netherlands interdisciplinary guidelines are available like the “Zorgstandaard CVA/TIA”⁶¹ and “Diagnostiek, behandeling en zorg voor patiënten met een beroerte.”⁶² However, these guidelines do not provide a detailed description of the evidence for the content of physical therapy in stroke rehabilitation, like diagnostics including prognosis, evidence for therapeutic interventions in the domain of physical therapy, and the use of health measurement instruments in the light of the clinical decision making process. The lack of discipline-specific evidence does not only apply to physical therapy, but also to other disciplines. Therefore, each discipline should take the responsibility to keep their discipline-specific evidence up to date. In the case of physical therapy, physical therapists should have access to up-to-date discipline-specific guidelines, to incorporate the best available evidence in daily practice.

The first Dutch national Clinical Practice Guideline for physical therapy in patients with stroke (*KNGF-guideline Stroke*) of the Royal Dutch Society for Physical Therapy (Koninklijk Nederlands Genootschap voor Fysiotherapie; KNGF) by Van Peppen et al.⁶³ was launched in 2004. With stroke rehabilitation as being one of the fastest growing fields in stroke research,⁶⁴ an update of this guideline was urgently needed. Not only the increased number of published RCTs and anticipated shifts in evidence and direction prompted the need for an update. Also the increase in scientific knowledge about functional prognosis and its determinants, and a call from the professional field to critically review the recommended measurement instruments were reasons to update the national guideline. With a grant of the KNGF (grant number 8091.1), the *KNGF-guideline Stroke* was revised from December 2010 till November 2013. The outline for this guideline follows the cyclic therapeutic process mentioned above (see section “*stroke care and complex rehabilitation interventions*”), in which the update of the evidence for interventions in the domain of physical

therapy poststroke is a comprehensive section. The selected approach is broadly consistent with the generally accepted important components of guideline development: (1) involvement of a panel of experts who develop the guideline and who do not have conflicts of interest; (2) a transparent systematic search for evidence (broad, extensive, also unpublished sources, to exclude bias as much as possible); (3) transparent grading the evidence and formulating recommendations; (4) consideration of clinical application/feasibility; 5) external peer review; and 6) frequent updating the guideline.^{65,66}

EVIDENCE-BASED INTERVENTIONS IN POSTSTROKE PHYSICAL THERAPY

To delineate a broad overview of the evidence for interventions poststroke fitting into the domain of physical therapy, the state of the art concerning these interventions is described in **chapter 5**. This chapter forms the basis of the section relating to therapeutic interventions in the revised *KNGF-guideline Stroke*.^{63,67}

Two essential aspects of effective motor rehabilitation interventions are intensity of training in terms of time and task-specificity (or: task-oriented training).^{23,68,69} A systematic quantitative literature overview published in 2004 showed that patients poststroke benefit from more time spent in exercise therapy when compared to less time spent in exercise therapy.⁷⁰ These positive small effects were related to exercise therapy focused on the lower limb and basic ADL, concerned a treatment contrast amounting 16 hours, and were restricted to the first 6 months poststroke. In order to update these findings, **chapter 6** describes a systematic review of the literature and meta-analyses for intensity of exercise therapy poststroke, with a focus on lower limb exercise interventions without the use of extensive equipment applied within the first 6 months after onset.

For the upper limb, original constraint-induced movement therapy (CIMT) and its modified versions are stroke rehabilitation interventions that capture both features of intensity and task-specificity. The protocol for original CIMT is characterized by three components: (1) repetitive, task-oriented training of the paretic upper limb according to the principles of shaping and task practice for 6 hours a day on 10 consecutive working days; (2) a transfer package, including adherence-enhancing behavioral strategies to facilitate the transfer of the in the laboratory setting practiced to daily life situations; and (3) constraining use of the less affected upper limb for 90% of the waking hours to stimulate the use of the more affected upper limb.⁷¹ Modified CIMT mainly applies two of these packages, with a reduced intensity. An intervention related to CIMT is forced use therapy, which solely includes constraining use of the less affected upper limb. With forced use, structured task-

specific training is therefore lacking. In **chapter 7**, a review is presented in which the evidence for original CIMT, its modified versions, and forced use is described not only post intervention, but also in the long term. In addition, a possible moderating effect of timing poststroke and dose-matching of intervention trials was investigated. Furthermore, hypothetical working mechanisms of these interventions were described.

APPLYING THE COLLECTED EVIDENCE

Identifying and analyzing scientific research in physical therapy in stroke rehabilitation serves several goals. First of all, to improve quality of care by translating scientific evidence into guideline recommendations for implementation in physical therapists' daily practice. Second, to guide the development of a scientific research agenda in collaboration with multiple stakeholders,⁷² which subsequently aids grant desks in determining priorities in grant allocation. Third, to assist politicians and policymakers in devising health care policies. And last but not least, to help patients with stroke and their caregivers in for example creating realistic expectations of rehabilitation outcomes or stroke care delivery and in critically assessing the consumed health care. For the latter, translation of scientific knowledge into an easily understandable message is necessary.

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