Stroke care in Sweden

Hospital care and patient follow-up based on Riks-Stroke, the National Quality Register for Stroke Care

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In Sweden, stroke care requires more bed days in hospitals and rehabilitation facilities than any other somatic illness. In 1994, Riks-Stroke (RS), the Swedish National Quality Register for Stroke Care, was started. The aim of RS is to monitor the quality of stroke management and to improve stroke care by providing comparative feed-back data on process and outcome. From 1998, the register covers all hospitals in Sweden admitting patients with acute stroke.

Annually approximately 20,000 stroke events have been included in RS which is estimated to be three quarters of all stroke events in Sweden. The coverage of stroke patients and the selection of patients included vary between hospitals, counties and regions. Results have to be interpreted in consideration to missing patients and case mix. Our validation studies of the national sample in RS show that stroke patients who were not included in RS more often had an uncertain stroke diagnosis and were less often treated in stroke units. They tended to be younger, less dependent in ADL functions before stroke, and they tended to cause an underestimate of the case fatality rates in RS.

An in-depth study of sex differences in RS showed that women with stroke were more often living in institutions three months after stroke. This was partly explained by a worse pre-stroke condition, differences in co-morbidities and need and distribution of help and support. RS is also a valuable tool for evaluation of the effectiveness of interventions in routine clinical practice. A large number of controlled randomised studies on stroke unit care have been performed, and the present study confirmed long-term beneficial effects in routine clinical practice. After considerations for selection and case-mix the national variations in stroke management can be studied. Although oral anticoagulants are recommended as first-choice in the primary and secondary prevention of stroke in patients with atrial fibrillation in the National Guidelines for Stroke Care, there have been wide variations not only between hospitals, but also between counties and health care regions. Local factors, general attitudes and traditions seem to be the major determinants of the use of oral anticoagulants in stroke patients with atrial fibrillation. RS is a valuable resource for follow-up studies of long-term consequences. Post-stroke fatigue is a frequent and unexplored long-term consequence after stroke. Post-stroke fatigue was found to be an independent predictor for functional dependence, institutional living and death two years after stroke.

In conclusion, the interest for and development of stroke care has increased dramatically the last decades. RS has contributed to this development by providing tools for monitoring of stroke care. Our study shows that RS is representative for stroke care in Sweden. There are variations in management and outcome in Swedish stroke care, and many patients suffer from long-term consequences, indicating that there is still considerable room for improvements in stroke care.

Key words: stroke care, quality register, routine clinical practice, validation, sex differences, stroke units, atrial fibrillation, oral anticoagulants, post-stroke fatigue
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Umeå 2003
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ADL</td>
<td>Activities of Daily Living</td>
</tr>
<tr>
<td>AF</td>
<td>Atrial Fibrillation</td>
</tr>
<tr>
<td>BFI</td>
<td>Brief Fatigue Inventory</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>CF</td>
<td>Case Fatality</td>
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<tr>
<td>CT</td>
<td>Computerised Tomography</td>
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<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
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<tr>
<td>INR</td>
<td>International Normalised Ratio</td>
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<tr>
<td>GW</td>
<td>General Ward</td>
</tr>
<tr>
<td>NDR</td>
<td>The Swedish National Discharge Register</td>
</tr>
<tr>
<td>NNT</td>
<td>Numbers Needed to Treat</td>
</tr>
<tr>
<td>OA</td>
<td>Oral Anticoagulants</td>
</tr>
<tr>
<td>OR</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td>RS</td>
<td>The Riks-Stroke register</td>
</tr>
<tr>
<td>RIKS-HIA</td>
<td>The Register of Information and Knowledge about Swedish Heart Intensive Care Admissions</td>
</tr>
<tr>
<td>RLS</td>
<td>Reaction Level Scale</td>
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<tr>
<td>SAH</td>
<td>Subarachnoid Haemorrhage</td>
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<tr>
<td>SD</td>
<td>Standard Deviation</td>
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<tr>
<td>SKAR</td>
<td>The Swedish Knee Arthroplasty Register</td>
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<tr>
<td>SU</td>
<td>Stroke Unit</td>
</tr>
<tr>
<td>SUTC</td>
<td>Stroke Unit Trialist’s Collaboration</td>
</tr>
<tr>
<td>TIA</td>
<td>Transient Ischaemic Attack</td>
</tr>
<tr>
<td>THA</td>
<td>The Swedish National Total Hip Arthroplasty Register</td>
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<td>WHO</td>
<td>World Health Organisation</td>
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</table>
### DEFINITIONS

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age standardisation</td>
<td>The crude specific rates are recalculated to what they would have been in the study population if that population had the same age distribution as the standard population.</td>
</tr>
<tr>
<td>Case fatality rate</td>
<td>The proportion of all cases which are fatal within a specified time.</td>
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<tr>
<td>Confidence interval</td>
<td>The range of values for a variable of interest, constructed so that the range has a specified probability of including the true value of the variable.</td>
</tr>
<tr>
<td>Disability</td>
<td>Temporary or long-term reduction of a person's capacity to function.</td>
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<tr>
<td>Incidence</td>
<td>The rate at which new events occur in a population. The numerator is the number of new cases in a defined period and the denominator is the population at risk of experiencing the event during this period. In this thesis, the term incidence means first-ever strokes.</td>
</tr>
<tr>
<td>Mortality</td>
<td>An estimate of the proportion of a population that dies during a specified period.</td>
</tr>
<tr>
<td>Odds</td>
<td>The ratio of the probability of the occurrence to non-occurrence of an event.</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>The ratio of two odds.</td>
</tr>
<tr>
<td>Prevalence</td>
<td>The number of persons with a disease or other conditions in a given population at a designated time.</td>
</tr>
<tr>
<td>Regression analyses</td>
<td>Given data on a dependent variable y and one or more independent variables $x_1$, $x_2$, etc., regression analysis involves finding the “best” mathematical model to describe $y$ as a function of the $x$'s, or to predict $y$ from the $x$'s.</td>
</tr>
<tr>
<td>Risk factor</td>
<td>This is a factor that is positively associated with the risk of developing the disease, but it does not necessarily cause the disease. The association should also be strong and dose-related if it is a continuous variable, such as blood pressure.</td>
</tr>
<tr>
<td>Reliability</td>
<td>The degree of stability exhibited when a measurement is repeated under identical conditions.</td>
</tr>
</tbody>
</table>
Sensitivity
The proportion of truly diseased persons in the population who are identified as diseased by the test. A measure of the probability of correctly diagnosing a case.

Specificity
The proportion of truly non-diseased persons in the population which is identified as non-diseased with a test. A measure of correctly identifying a non-diseased person with a test.

Validity, measurement
The extent to which the instrument measures the concept it purports or is intended to measure.

Validity, study
The degree to which the inference drawn from a study, especially generalisations extending beyond the study sample, are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn.

The definitions have mainly been collected or revised from James M. Last (Ed) “A Dictionary of Epidemiology”, Oxford University Press, New York 1995.
ABSTRACT

In Sweden, stroke care requires more bed days in hospitals and rehabilitation facilities than any other somatic illness. In 1994, Riks-Stroke (RS), the Swedish National Quality Register for Stroke Care, was started. The aim of RS is to monitor the quality of stroke management and to improve stroke care by providing comparative feedback data on process and outcome. From 1998, the register covers all hospitals in Sweden admitting patients with acute stroke.

Annually approximately 20,000 stroke events have been included in RS which is estimated to be three quarters of all stroke events in Sweden. The coverage of stroke patients and the selection of patients included vary between hospitals, counties and regions. Results have to be interpreted in consideration to missing patients and case mix. Our validation studies of the national sample in RS show that stroke patients who were not included in RS more often had an uncertain stroke diagnosis and were less often treated in stroke units. They tended to be younger, less dependent in ADL functions before stroke, and they tended to cause an underestimate of case fatality rates in RS.

An in-depth study of sex differences in RS showed that women with stroke were more often living in institutions three months after stroke. This was partly explained by a worse pre-stroke condition, differences in co-morbidities and need and distribution of help and support. RS is also a valuable tool for evaluation of the effectiveness of the interventions in routine clinical practice. A large number of controlled randomised studies on stroke unit care have been performed and the present study confirmed long-term beneficial effects in routine clinical practice. After considerations for selection and case-mix the national variations in stroke management can be studied. Although oral anticoagulants are recommended as first-choice in the primary and secondary prevention of stroke in patients with atrial fibrillation in the National Guidelines for Stroke Care, there have been wide variations not only between hospitals, but also between counties and health care regions. Local factors, general attitudes and traditions seem to be major determinants of the use of oral anticoagulants in stroke patients with atrial fibrillation. RS is a valuable resource for follow-up studies of long-term consequences. Post-stroke fatigue is a frequent and unexplored long-term consequence after stroke. Post-stroke fatigue was found to be an independent predictor for functional dependence, institutional living and death more than two years after stroke.

In conclusion, the interest for and development of stroke care has increased dramatically during the last decades. RS has contributed to this development by providing tools for monitoring stroke care. Our study shows that RS is representative for stroke care in Sweden. There are variations in management and outcome in Swedish stroke care and many patients suffer from long-term consequences, indicating that there is still considerable room for improvements in stroke care.

Key words: stroke care, quality register, routine clinical practice, validation, sex differences, stroke units, atrial fibrillation, oral anticoagulants, fatigue
LIST OF ORIGINAL PAPERS


1 BACKGROUND

1.1 Stroke in Sweden

About 30,000 to 35,000 patients suffer each year from strokes in Sweden, leading to a prevalence, i.e., the proportion of stroke-affected persons in Sweden at a given time, of more than 100,000 people\(^1\). Of all strokes, the proportion with a first-ever stroke is around 80\% in ages below 75\(^2\) and 73-77\% in all ages\(^3,4\). The mean age of stroke patients in Sweden is 75 years\(^5\).

The prevalence is determined by the incidence, i.e., the rate at which a new event occurs in a population, and the proportion of all cases dying within a specified time, i.e., case fatality. The age-specific incidence has not changed for a long time in Sweden\(^6\). However, the risk of being affected by stroke increases with increasing age. With a growing population of elderly and an unchanged age-specific incidence, the total incidence will increase. In addition, more patients will survive their strokes and subsequently the absolute number of stroke-affected persons in Sweden will increase\(^6\). Despite the expected increase in the total number of stroke events, the decrease in case fatality seen during the past years will lead to a decrease in the total number of stroke deaths in Sweden\(^7,9\). Subsequently, there will be more stroke patients who are in need of health care, rehabilitation, and help and support in daily living. The demands on health care and the society as a whole will increase.

1.2 Stroke care in Sweden

Stroke care utilises a large share of health services in Sweden, requiring more bed days in hospitals and rehabilitation facilities than any other illness\(^10\). Figure 1 shows the number of hospital admissions with stroke diagnosis and mean length of stay for each hospital admission during 1998 to 2000, as emerges from routine health statistics. The same information, but sub-grouped for intracerebral haemorrhage, cerebral infarction and unspecified stroke is shown for 2000 in Table I. The total
cost of stroke in Sweden each year was estimated in 1997 to be 13.5 billion Swedish crowns of which the hospital care is responsible for 8.4 billion.

Stroke care in Sweden involves county health care, comprising hospital health care and primary health care and municipal care. The counties and the municipals have parallel local autonomy and have responsibility for structuring and developing different parts of health care and social services. The counties are organised by the Federation of County Councils and the municipals by the Federation of Municipals. On the state level, the Ministry of Health and Social Affairs is main responsible for development of health care and social issues. The National Board of Health and Welfare is a Swedish government agency and is responsible for monitoring, evaluation and supervision of health care and social services.

Earlier studies have shown that 90-97% of patients with acute stroke in Sweden are treated in hospitals during the acute phase. The hospitals have geographically based catchment areas and are organised into 20 counties with at least one county hospital in each. These counties are then divided into 6 health care regions with regional hospitals, which usually also serve as university hospitals. The regional health care is more specialised and regulated by agreements between those counties concerned.
Table 1. Total number of hospital admissions and mean length of stay by routine health statistics in 2000 (ICD-10: I61, I63, I64). National Discharge Register at National Board of Health and Welfare.12

<table>
<thead>
<tr>
<th></th>
<th>Total number of hospital admissions</th>
<th>Mean length of stay</th>
</tr>
</thead>
<tbody>
<tr>
<td>I61 Cerebral haemorrhage</td>
<td>4,854</td>
<td>15.6</td>
</tr>
<tr>
<td>I63 Cerebral infarction</td>
<td>29,176</td>
<td>13.6</td>
</tr>
<tr>
<td>I64 Unspecified stroke</td>
<td>3,866</td>
<td>10.3</td>
</tr>
</tbody>
</table>

In 1992, the “Ädel-reform” was performed. Responsibility and resources for care in long-term settings were transferred from county health care to municipal care. In other words, the impact of municipal care, on the care of elderly increased. Because the mean age of stroke patients is 75 years and more elderly are in need of long-term care, the “Ädel-reform” concerns stroke patients and stroke care as well. Before the reform, stroke patients spent just over 3 million hospital treatment days in hospital each year, of which 2.5 million were in geriatric/long-term facilities. In 2000, 500,000 treatment days were spent in hospitals. Besides ensuring a high and consistent quality of county health care and municipal care separately, the organisation of an efficient chain of care with clear definitions of responsibility, involving both county health care and municipal care, is a challenge for now and the future.

1.3 National quality registers

The importance of establishing national databases for specific diagnoses as part of the quality assurance system was noted in the 1996-1999 year "Dagmar Agreement" between the Ministry of Health and Social Affairs and the Federation of Swedish County Councils.16,17 Resources for development of national quality registers are allocated within the framework of this agreement. In Sweden there are now approximately 50 national registers monitoring quality of different aspects of health care. The registers are heterogeneously organised but most were started by representatives from the medical profession and serve local interests and have gradually increased to cover a national perspective. On a national level, the registers are supported and coordinated by a Steering Committee of representatives from the Swedish Society of Medicine, the Federation of Swedish County Councils and the National Board of Health and Welfare.18

Because of the considerable impact that stroke has and will have on health care in Sweden in the future, a joint council on quality of
the Swedish Society of Medicine, the Swedish Medical Association, and
the Swedish Association for Internal Medicine, has identified stroke as a
marker diagnosis that gauges the general quality of health care in
Sweden. Riks-Stroke (RS), the Swedish national quality register for
stroke care, was started in 1994. The establishment of a national quality
register for stroke was also stimulated by the Helsingborg declaration, a
consensus document developed in 1995 by WHO and the European
Stroke Council. The declaration included a recommendation to establish
routine collection of data for evaluation of quality of stroke care 19.

The aim of RS is to monitor the quality of stroke management
to improve stroke care by providing comparative feed-back data on
process and outcome 5. From 1998, the register covers all hospitals in
Sweden admitting patients with acute stroke. A computerised data
registration sheet is used and local data are submitted by an Internet-
based system to the national data management centre of RS. Each
participating hospital receives online feed-back information on the local
hospital data. The results from each individual hospital are compared
with the distribution of the summarised national data.

Sweden is the first country with a monitoring system for stroke
care that has a national coverage. Several other countries have started to
establish similar systems. Norway is monitoring stroke care in a
restricted geographical area and is in the future planning to expand to a
national monitoring system. In Canada, the Canadian Stroke System
Coalition promotes a system for prevention and control of stroke 20.
Parallel to optimising stroke prevention, pre-hospital and emergency
care, hospital care, rehabilitation, and reintegration into community, the
Canadian Stroke System has a surveillance system that is a part of
routine stroke management. As with RS, the information should be
available to health care planners on all levels. Several other countries are
also aiming to establish national monitoring systems for stroke care. The
Scottish Stroke Outcome Study Group performed a study on 5 hospitals
where they revealed statistically significant differences in case fatality,
even after case mix adjustments 21. A direct monitoring would identify
hospitals with major shortcomings as well as moderate, but clinically
important variations between hospitals. In the US, the Centers for
Disease Control and Prevention have gathered an expert group to
recommend a prototype for the Paul Coverdell National Acute Stroke
Registry 22.

The controlled randomised study is the commonly accepted
method for studying new interventions in health care. If shown effective,
the new procedure is then implemented in routine health care. However,
the beneficial effects seen in these studies are often diluted when the
intervention is transferred into routine health care. There are several
reasons for the diminished effect. Patients and stroke units (SUs) in
routine health care are more heterogeneous than in controlled studies.
Less strict adherence to criteria for patient selection and less well-defined interventions also contribute. As the national quality registers aim to measure routine health care in a national perspective, they are valuable tools for evaluation of effectiveness of the interventions in routine clinical practice.

1.4 Register validation

To ensure that RS reflects the stroke population treated in hospital in Sweden, the validity of the data need to be studied. A summary of the findings in validation studies performed during the first years of RS is presented in this thesis. There are several definitions and sub-classifications of validity. Validity can be defined as “the extent to which the instrument measures the concept it purports or is intended to measure”.

When measuring the validity of a questionnaire there are several types of validity that have to be assessed. The face validity measures how well the questionnaire appears to measure what it is supposed to measure. This is often tested on persons without knowledge in the field. Those with expertise test the content validity, how well the questionnaire incorporates the domains of the phenomenon. Still, it is an evaluation on how well the questionnaire appears to be. The face and the content validity have been tested continuously during those eight years the RS register has been operating in practice. Adjustments for improvements have been performed along the way. The criterion validity measures the extent to which the questionnaire correlates to other questionnaires, which are considered to be “golden standards”. The criterion validity is sub-classified into concurrent validity (same point in time) and predictive validity (ability to predict the phenomenon studied). The construct validity refers to a theoretical concept concerning the relevant phenomena. This construct validity is usually not possible to evaluate until after several years of experience have accumulated.

For validation of a register there are no well-established methods. Main issues to take into considerations are coverage, i.e., completeness of the register, and the quality of register data, i.e., how well the data included in the register agree with what is supposed to be included. In 1986 a method in which these two aspects of validity were taken into consideration was presented. The case validity measures the ascertainment of cases or if the register includes those patients intended to be included. The coverage of RS, or proportion of stroke patients treated in-hospital who are included, should be as complete as possible.
However, the crucial issue is the question of RS patients being representative for the stroke population treated in hospitals in Sweden. The item validity, according to Stone, measures the completeness and accuracy of individual items of data in the register as compared with an external source. RS data are compared with information in hospital records.

Other Swedish national quality registers have performed studies on validity of their data. RIKS-HIA, the Register of Information and Knowledge about Swedish Heart Intensive Care Admissions, assessed the item validity. They concluded that the register showed a 94% agreement between register data and information in hospital records. RIKS-HIA, the Register of Information and Knowledge about Swedish Heart Intensive Care Admissions, assessed the item validity. They concluded that the register showed a 94% agreement between register data and information in hospital records. The Swedish Knee Arthroplasty Register (SKAR) assessed the case validity by a postal questionnaire about knee revisions to all patients with a knee operation that was recorded in SKAR. The Swedish Knee Arthroplasty Register (SKAR) assessed the case validity by a postal questionnaire about knee revisions to all patients with a knee operation that was recorded in SKAR. The frequency of missing revision operations was 1.7%. With a comparison with national discharge data, 84% of missing revisions would have been identified. The most extensive study of data quality was performed by the Swedish National Total Hip Arthroplasty Register (THA). They showed a high validity as well as a high reliability for the questionnaires used. The case validity of the register showed that in comparisons with the National Discharge Register (NDR) and a postal questionnaire, 6% of revisions were missing in the THA. The National Death Register showed that there were no differences in 10-year survival in the national discharge cohort and the THA cohort.
1.5 Stroke and gender

1.5.1 Epidemiology

The prevalence of stroke has been shown to be higher among men than women in ages below 80 years \(^{31-34}\). However, in ages above 80, women have a higher prevalence \(^{31-34}\), although they have a lower age specific incidence \(^{2,4,35,36}\) and an assumed higher case fatality \(^{2,8,37,38}\). This is attributed to the general longevity of women, or a higher mortality among elderly men. In the elderly stroke population, more men have died from other causes leaving two thirds of stroke survivors in ages above 80 years being women \(^{32}\).

1.5.2 Outcome

In the literature, gender differences in pre-stroke condition, management and outcome after stroke are still controversial, and previously published studies have shown diverse results. Table 2 shows case fatality and functional outcome for men vs. women in several previously published studies.

1.5.3 Risk factors

Equal numbers of men and women are registered in RS each year although more men have experienced a previous stroke. Male gender has been shown to be associated with stroke recurrence \(^{3}\). A previous stroke is one of the strongest risk factors for a new stroke event \(^{39}\), and men are subsequently at a higher risk for a new stroke.

The risk factors associated with stroke are generally the same in men and women \(^{40}\). In many populations, a diagnosis of diabetes and the habit of smoking are more common among male stroke patients \(^{41}\), although these risk factors may have a stronger impact in women \(^{42-44}\). The relative risk for stroke is the same for hypertensive women as for hypertensive men \(^{45}\), although, hypertension has been found to be more frequent among women affected by stroke, \(^{41}\) implying a higher absolute risk for stroke.
Table 2. Stroke outcome in men vs. women in previously published studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case fatality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thorvaldsen et al. 1995 (^{2})</td>
<td>2,8</td>
<td>28-day case fatality rates higher among women in 15 out of 18 WHO MONICA populations.</td>
</tr>
<tr>
<td>Stegmayr et al. 1994 (^{8})</td>
<td>6,083</td>
<td>Women had a higher 28-day case fatality rate.</td>
</tr>
<tr>
<td>Nakayama et al. 1994 (^{46})</td>
<td>515</td>
<td>Sex was not a significant predictor for death within 3 months after stroke.</td>
</tr>
<tr>
<td>Moulin et al. 1997 (^{38})</td>
<td>2,500</td>
<td>Female gender was an independent predictor for in-hospital death.</td>
</tr>
<tr>
<td>Holroyd-Leduc et al. 2000 (^{41})</td>
<td>44,832</td>
<td>One-year case fatality rates higher for men.</td>
</tr>
<tr>
<td>Weimar et al. 2002 (^{47})</td>
<td>1,754</td>
<td>Gender did not predict death within 100 days from stroke onset.</td>
</tr>
<tr>
<td>Arboix et al. 2001 (^{48})</td>
<td>967</td>
<td>Women had higher in-hospital mortality</td>
</tr>
<tr>
<td>Sharma et al. 2002 (^{49})</td>
<td>296</td>
<td>No differences in case fatality rates. Minor tendency for higher acute phase case fatality rates for women.</td>
</tr>
<tr>
<td><strong>Functional outcome</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jongbloed et al. 1986 (^{50})</td>
<td></td>
<td>A critical review showed no relationship between sex and functional outcome after stroke.</td>
</tr>
<tr>
<td>Nakayama et al. 1994 (^{46})</td>
<td>515</td>
<td>Sex was not a significant predictor for functional outcome in the study.</td>
</tr>
<tr>
<td>Wyller et al. 1997 (^{51})</td>
<td>165</td>
<td>Men had better motor function, cognitive function and ADL function one year after stroke.</td>
</tr>
<tr>
<td>Löfgren et al. 1998 (^{52})</td>
<td>99</td>
<td>Male sex was an independent predictor for ADL improvement.</td>
</tr>
<tr>
<td>Lai et al. 1998 (^{53})</td>
<td>662</td>
<td>Gender was not a significant predictor for being sent back home.</td>
</tr>
<tr>
<td>Weimar et al. 2002 (^{47})</td>
<td>1,754</td>
<td>Female sex was an independent predictor for functional dependence 100 days after stroke.</td>
</tr>
<tr>
<td>Holroyd-Leduc et al. 2000 (^{41})</td>
<td>44,832</td>
<td>Men were more likely to be discharged home.</td>
</tr>
<tr>
<td>Appelros et al. 2003 (^{54})</td>
<td>377</td>
<td>Gender was not an independent predictor for functional dependence.</td>
</tr>
</tbody>
</table>
The prevalence of atrial fibrillation (AF) is higher among men in all age-groups, although the difference diminishes with age. Because of the longevity of women, the absolute number of men and women with AF is about the same. Several studies have shown that women with AF are less often treated with oral anticoagulants (OA) as primary stroke prevention. This may seem paradoxical since women with AF have as high a risk for embolism and long-term mortality as men, and the beneficial effect of OA has been shown to be even greater among women. Women with AF are older and have more often co-morbidity. Therefore, they may have an increased risk of complications and are in need of a more careful monitoring of anticoagulant intensity.

1.5.4 Medical management

Women have been shown to have more non-traditional stroke symptoms, such as pain and change in level of consciousness, at stroke onset as compared with men. These sex differences may have implications for discrepancies in acute management of male vs. female stroke patients. Sex differences in various aspects of medical management of stroke have been scarcely studied. In one of the few studies performed, female patients with cerebral infarction had fewer angiograms and carotid endarterectomies as compared with male patients. However, this was mainly because of a higher occurrence of carotid disease in men. Among patients who undergo a carotid endarterectomy, women with asymptomatic stenoses have a higher risk for early complications, while the risk for complications is the same for men and women when they suffer from symptomatic stenosis.

Meta-analyses have not shown any differences in beneficial effect of SU care between men and women. However, female patients are older, and as shown above, they may suffer from more severe strokes. Because SU care lowers the risk for complications after stroke, patients with severe strokes have a marked benefit from treatment in SUs. When older patients with severe strokes do not receive SU care, female patients are probably more severely affected.

Current evidence and recommendations support equal treatment strategies for stroke prevention for men and women. Previously published studies have shown that elderly female stroke survivors received treatment with antiplatelet agents less often than elderly men who have had a stroke. The authors speculate that the higher proportion with disability and institutional living among women might be one reason for differences in strategy of secondary prevention.
1.5.5 Depression and social situation

Depression after stroke is very common and affects survival as well as functional outcome and life satisfaction after stroke\textsuperscript{67-70}. In the general population, depression is more common among women\textsuperscript{71}. Whether female stroke survivors also are more affected by depression is controversial. In one study, it was shown that women were twice as often diagnosed with major depression two weeks after stroke\textsuperscript{72}. The increased frequency of depression in female stroke patients has been shown to persist at six months and one year after stroke\textsuperscript{73}. However, a Swedish study showed no relationship between gender and post-stroke depression\textsuperscript{70}. The mechanisms causing post-stroke depression have been suggested to differ between men and women\textsuperscript{72}. In women, post-stroke depression is associated with a history of psychiatric disease and cognitive impairment. Left-sided lesions have also been shown to be more common among women. However, a meta-analysis could not find any evidence for an association between left-sided lesions and post-stroke depression\textsuperscript{74}. In men the depression was associated with functional dependency and social impairment. These differences might have implications for treatment.

Several studies have shown that women who have had a stroke have more disability and are more frequently living in institutions. Impaired physical and mental capacities are not the only factors that predict transition to institutional living. Good social support counteracts this process and is associated with faster and more extensive recovery of functional status after stroke\textsuperscript{75}. Large social networks lower the risk for institutionalisation\textsuperscript{76}. Elderly patients have been shown to be placed in an institutional living despite a relatively good functional ability because of inadequate social support\textsuperscript{50,77}. Because more elderly women are living alone they probably have less social support than men.
1.6 Organised stroke care

1.6.1 Definition of stroke unit

There are several types of organised stroke care and there are several different definitions of a SU. The Stroke Unit Trialists’ Collaboration (SUTC) have defined a SU as “organised specialist in-patient stroke care” 64, 78. The most well known is the dedicated SU where service is dedicated exclusively to the care of stroke patients. There are several different subtypes of organised stroke care and Table 3 shows their characteristics. Patients treated in general wards (GW) are mostly used as control group in randomised studies of SU care.

Results from RS indicate that 70% or less of stroke patients in Sweden receive treatment in a SU. Most SUs are dedicated SUs but all types of organised stroke care described above are represented.

1.6.2 Stroke units and effect on outcome

A meta-analysis of randomised studies, performed by the SUTC, showed that SU care improves survival and functional outcome after stroke 64, 78. The odds ratio for long-term reduction of death was 0.83 (95% CI 0.69-0.98), for combined outcome death or dependency 0.69 (95% CI, 0.59-0.82) and for death or institutionalisation 0.75 (95% CI, 0.65-0.87). The Numbers Needed to Treat (NNT) to prevent one death was 25, and NNT to enable one extra person to return home independently was 20 78. The benefit was not shown to be restricted to any subgroup of patients or model of stroke care organisation. Although the beneficial effect of organised stroke care has been well established, there are marked differences between individual studies. Some studies show no effect and others show a dramatic effect 79-82. Variations in outcome may be explained by differences in study population, type of organised stroke care and study design.

In the previously mentioned meta-analysis on how SUs improve stroke outcome, SU care was shown to benefit all patients independently of stroke severity 65. In patients with mild strokes, more patients treated in SUs tended to gain functional independence. In patients with moderately severe strokes, SU care resulted in positive trends in survival and independence, fewer days in-hospital and in
Table 3. Definitions of subtypes of stroke units and their characteristics

<table>
<thead>
<tr>
<th>Subtype of organised stroke care</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive-care stroke units</td>
<td>➢ Accepts patients acutely but discharge early, often within 2-7 days</td>
</tr>
<tr>
<td></td>
<td>➢ Continuos monitoring and treatment of complications</td>
</tr>
<tr>
<td></td>
<td>➢ Super acute treatments such as thrombolysis</td>
</tr>
<tr>
<td>Rehabilitation stroke units</td>
<td>➢ Accepts patients after the acute care, usually a delay of 7 days or more.</td>
</tr>
<tr>
<td></td>
<td>➢ Focus on stroke rehabilitation</td>
</tr>
<tr>
<td>Non-intensive stroke units</td>
<td>➢ Combination of intensive care and rehabilitation stroke units.</td>
</tr>
<tr>
<td></td>
<td>➢ Accepts patients acutely for early diagnosis, super acute treatments of stroke and treatment of complications.</td>
</tr>
<tr>
<td></td>
<td>➢ Focus on early mobilisation, short- and long-term rehabilitation</td>
</tr>
<tr>
<td>Mixed rehabilitation wards</td>
<td>➢ Wards with multidisciplinary teams that focus on rehabilitation, but not exclusively stroke rehabilitation</td>
</tr>
<tr>
<td>Stroke team care</td>
<td>➢ Multidisciplinary teams specialised in stroke care. Providing care in any ward throughout the hospital</td>
</tr>
</tbody>
</table>

Institutional care. The beneficial effect in patients with severe stroke was both in terms of improved survival and in a higher proportion of patients being functionally independent. In many studies, elderly patients and patients with severe strokes were excluded. In a Norwegian SU trial performed by Indredavik et al., patients who were treated in SUs had better outcome, but patients who lived in nursing homes before the stroke were excluded. Results from one earlier study that included a more heterogeneous study population suggested that the beneficial effects of treatment in SUs might be less pronounced for elderly and more severely disabled patients. Other studies have not shown any differences in beneficial effect of treatment in SUs between subgroups, and results from these studies support the contention that SUs should treat an unselected population of stroke patients. Variations in effect on stroke outcome according to stroke subtype have, in one study, shown that SU care improves outcome in patients with large-vessel infarcts but not for lacunar infarct patients.
Improvement in other types of outcome, beside survival and physical impairment, has also been studied. Indredavik et al. 89 and Juby et al. 90 published studies that focused on differences in quality of life between patients treated in SUs and in GWs. Indredavik showed statistically significant differences in all aspects of the Nottingham Health Profile 90 except for pain. In the study performed by Juby, patients treated in SUs showed better psychological outcome.

1.6.3 What makes stroke units effective?

Although several studies and meta-analyses have shown a beneficial effect of SU care, the essential components of care have not been clearly understood. In particular, the components of stroke rehabilitation, as compared with medical interventions, are more difficult to evaluate and apply to evidence-based practice 91, 92. However, it has been shown that organised in-patients multidisciplinary post-acute stroke care has a beneficial effect on outcome 93. Observational studies have shown that patients in SUs spend more time out of bed and in interaction with nurses and therapists 94, 95. The Trondheim SU trial showed that early mobilisation/training and stabilisation of diastolic blood pressure were independently associated with the chance of being discharged home 96. The impact of characteristics of the SU care, as multidisciplinary trained staff and involvement of relatives, are of importance but difficult to measure. A review on why SUs are effective identified similar approaches for several studies 97. In most studies, multidisciplinary teams were providing multiple interventions, and they were co-ordinated by multidisciplinary meetings. The care was characterised by: comprehensive assessment of medical problems, impairments and disabilities, active physiological management, early mobilisation, skilled nursing care, early setting of rehabilitation plans involving carers, and assessment and planning of discharge needs. These components are also cornerstones in recommendations of SU care in the Swedish National Guidelines for Stroke care 11.

It has been suggested that SUs in discrete wards are more efficient in reducing mortality, institutionalisation and dependency as compared with specialised stroke teams or specialist domiciliary care 98. In the SUTC meta-analysis, only one study on stroke-teams was included. No conclusions could be made on differences between stroke-team care and care in a discrete ward 78. Previously published studies have shown that 85% of all stroke patients have some type of complication during the hospital admission 99. Additional studies have shown that SU-care in combination with a more active strategy for prevention and treatment of complications is a major contributor to SUs beneficial effect on stroke outcome 100. The SUTC has shown that the beneficial effect on survival is most prominent between 1 and 3 weeks.
after the stroke. During this time period many of the complications after stroke are believed to occur. The main reason for patients being able to return home was the improved functional independence.

Economic analyses of SU care are difficult to perform. The cost of hospital-based stroke care, after adjustment for case mix, varies considerably across Europe. This variation is mainly due to differences in organisation of stroke care and use of resources. It has been shown that SUs do not increase the cost for stroke patients. The establishment of SUs may even release health care resources. To make stroke care cost-effective, establishment of SUs and multidisciplinary teams are the major issues. Stroke prevention with aspirin for all ischaemic stroke patients, OA for all ischaemic stroke patients with AF and risk factor interventions are essential components as well.

1.6.4 Stroke units in routine clinical practice

Although a controlled randomised study design has its advantages when studying the effect of a structured stroke care that is not confounded by other factors, there is a risk of a too strict selection of patients. The patients and methods might not be representative for a true clinical picture of the disease. Further, there is a question of large-scale applicability in routine clinical practice of interventions used by dedicated investigators in small, randomised trials. An attempt to answer this question was performed with data from RS, in a Norwegian single-centre study and in a study from Denmark. In the Norwegian study, among all stroke patients above the age of 60 allocated to an SU or a GW, treatment in an SU was an independent predictor for surviving 30 days after stroke onset. Beneficial effects of SU care, for an unselected group of stroke patients were found in the Danish study. In the RS study, the analyses on early survival and functional outcome were restricted to patients who had been living at home without any community support before the stroke. A beneficial effect from treatment in a SU was shown, but only for the subgroup of patients who were fully conscious on arrival at hospital.
1.7 Stroke prevention in patients with atrial fibrillation

1.7.1 Atrial fibrillation and risk for stroke

Atrial fibrillation is the most common supraventricular heart arrhythmia. The prevalence is 2-5% in the general population aged 60 or older. The incidence and the prevalence increase with age, and in the Framingham Heart Study, the prevalence of AF was 2% in persons 60-69 years of age and 9% in patients aged 80-89. Another study showed the same association between age and prevalence of AF although the age-specific prevalence was higher, 5% in persons between 60 and 70 years of age, 13% in persons between 71 and 91 and 22% in those between 91 and 103 years of age. In the Cardiovascular Health Study, the incidence of AF in ages 65 years or older, was 19.2 per 1000 person-years. The incidence rates showed an annual increase with age, from 0.2 per 1000 for ages 30-39 to 39.0 per 1000 for ages 80-89. The age-specific incidence of AF is higher in men than in women.

The Framingham Heart Study also showed that the risk for death from cardiovascular causes was 2.7 times higher in women, and 2.0 times higher in men with AF than in persons with sinus rhythm. AF was later shown to be independently associated with a 1.5-fold increase in mortality in men and a 1.9-fold increase in mortality in women even after adjustment for preexisting cardiovascular conditions.

AF is an important independent risk factor for stroke. The Framingham Heart Study showed that 15% of all strokes were associated with AF and the proportion of AF-associated strokes increased with age. The relative risk for stroke for a person with AF was 2.6 in patients between 60 and 69 years of age and increased to 4.5 in patients 80 to 89 years of age. The three-year incidence of stroke in a study population with a mean age of 81 years, was 38% in AF patients as compared with 11% in patients with sinus rhythm, showing a relative risk for stroke of 3.3. Age above 65, history of hypertension, diabetes and previous transitory ischaemic attack (TIA) or stroke have been shown to increase the risk for stroke in AF patients. Congestive heart failure or coronary artery disease increases stroke rate three times in AF patients. In addition, a left ventricular dysfunction together with an atrium greater than 2.5 cm/m² are associated with increased thromboembolism. A recently published study showed a correlation between clinical risk...
factors mentioned above and a thrombogenic milieu on transoesophageal echocardiography (presence of dense left atrial spontaneous echo contrast, left atrial appendage flow velocity ≤ 0.25 m/s, or both) \(^{119}\). Left ventricular ejection fraction <45% and age >65 were independent predictors of thrombogenic milieu. Patients with lone AF, i.e., below the age of 65, without pathological changes on echocardiogram or any risk factors, have only a 1% annual risk for stroke \(^{118}\). Patients with paroxysmal AF have been shown to have the same risk for stroke as patients with chronic AF \(^{120}\).

1.7.2 Oral anticoagulants as primary and secondary stroke prevention

In the primary prevention of stroke, anticoagulant therapy in patients with AF is one of the most effective strategies. Patients on treatment with OA have been shown to have a risk for stroke that is only one third that of patients on placebo (OR 0.30; 95% CI 0.19-0.48) \(^{121}\). Another pooled analysis showed similar reduction in stroke rate among AF patients treated with OA from 4.5% to 1.4% (68% risk reduction) \(^{116}\). Oral anticoagulants have been shown to be approximately 50% more effective than aspirin, which lowered the risk for stroke by 44% \(^{116}\). In the latest Cochrane review on the subject, the OR for stroke in patients with warfarin treatment was 0.64 (95% CI; 0.43-0.96) as compared with patients on aspirin \(^{121}\). The superiority of anticoagulation over antiplatelet treatment in the prevention of embolism has been reviewed also by other authors \(^{122,123}\). If the risk of severe bleeding complications is kept low, anticoagulation in AF patients is highly cost-effective, and it may actually save money for the community \(^{124,125}\).

Among AF patients who have already suffered an ischaemic stroke and receive anticoagulation or antiplatelet therapy, the risk of a recurrent stroke in the next five years has been reported to range from 20% to 37% \(^{66,126,127}\). In these patients, secondary prevention with OA seems to be highly effective. The data available show that compared with aspirin, anticoagulant therapy decreases the odds of recurrent stroke by two-thirds (OR 0.35; 95% CI 0.22-0.59) \(^{128}\).

The Swedish National Guidelines for Stroke Care categorises AF patients into three groups according to risk for embolic stroke, based on age and concomitant risk factors such as hypertension, diabetes, congestive heart failure, previous TIA or stroke, and echocardiographic risk markers \(^{129}\). Patients below the age of 60 with no other risk factors are not recommended to be treated with any antithrombotic stroke prevention. Patients 60-65 years of age who have no other risk factors have a low risk for embolic stroke and should receive aspirin, 75-325 mg/day. Oral anticoagulants are the first choice of treatment for patients who are 65 years or older and who have additional risk factors.
1.7.3 Variations in use of oral anticoagulants as stroke prevention

The effectiveness of OA for prevention of stroke in routine practice has been documented in several studies. Most of the studies have shown an equivalent effect in routine practice as compared with randomised trials. However, Frost et al. suggested the effect might be more moderate. Despite the compelling scientific evidence, there appears to be large variations in how OA is used to prevent first and recurrent strokes in clinical practice. For inpatients, outpatients and patients in long-term care settings, an underuse of OA has been shown. In contrast to these findings, Weisbord et al. showed that few AF patients who did not receive warfarin were without contraindications.

In a review of why patients with AF do not receive warfarin, Bungard et al. concluded that “physicians’s perception of the benefit vs. risk of therapy appears to be the only consistent finding influencing the implementation of warfarin therapy.” The benefit-risk assessment is influenced by several factors and differs between physicians. Age is one of the strongest determinants for the chance of receiving treatment with OA, both for primary and secondary prevention. Prevention of stroke in older patients is a challenge. In most randomised trials, older stroke patients are excluded. They have an increased risk of stroke and an increased risk of bleeding complications, and this risk stops many doctors from anticoagulating older patients. However, the intensity of anticoagulation may be a more important predictor for bleeding than age. To obtain an optimal treatment control and to minimise bleeding risk, these patients probably need a more careful monitoring. The dose to maintain treatment within therapeutic INR range decreases with age. Older patients also have a higher prevalence of other diseases and medications that influence the INR stability. Other co-morbidities such as hypertension and diabetes, in combination with AF, increase the risk for stroke and the risk of haemorrhagic complications. Oral anticoagulants as secondary prevention are even more important in this group of patients because older patients with AF and a previous stroke have an even greater risk for a stroke recurrence.

Treatment with OA needs continuous monitoring. Much effort has been spent on organising optimal management. If the treatment is organised by special hospital-based services or in general practice does not seem to be a crucial issue, as indicated in a study from Northern Sweden where the proportion of patients within treatment recommendations and proportion with treatment failure were similar in hospitals and health centres in this specific area. However, studies have suggested that treatment with OA should be managed in...
anticoagulation services \(^{170}\). In surveys of barriers to warfarin therapy, many physicians believe that monitoring therapy is inconvenient \(^{135},^{143}\). Better access to consultant advice would increase the use of OA because clinical uncertainty is also often reported in studies of how physicians manage patients with OA \(^{135},^{151}\). Many of these aspects are logistical issues that rest within organisation of health care.

1.7.4 Oral anticoagulants and haemorrhagic complications

A major bleeding and especially an intracranial bleeding is the feared complication of treatment with OA in patients with AF \(^{171}\). The frequency of major bleeding complications varies between studies although meta-analyses have shown that patients on OA have approximately twice the risk for bleeding than patients on placebo \(^{121},^{172}-^{174}\). The Cochrane meta-analyses showed an OR of 2.35 (95% CI; 1.20-4.24) \(^{121}\). The annual risk for intracranial bleeding is increased three times, from 0.1% to 0.3% \(^{116},^{174}\). In total, 30 strokes/1000 person-years can be prevented with warfarin at the expense of 6 major haemorrhages \(^{121}\). Stroke prevention with warfarin, showes an odds ratio for major bleeding of 1.8 as compared with treatment with aspirin (95% CI; 0.95-3.48) \(^{121}\).

The predictive factor for increased risk for major bleeding complications is, above all, intensity of anticoagulation \(^{175}\). Meta-analyses of warfarin treatment show that in the study with the highest bleeding rates, 17% of the measurements were above the target INR of 2.5-4.0 \(^{176}\) as compared with only 5% in the study with lowest bleeding rates \(^{174},^{177}\). The optimal range of anticoagulation therapy should be within INR 2.0 to 3.0 \(^{156},^{175},^{178}\). High INR is also associated with an increased risk for mortality \(^{179}\). Treatment with OA in elderly people has been discussed in previous section 1.6.3. Several other diseases, e.g., previous gastrointestinal bleeding, hypertension, diabetes, previous stroke, severe cardiovascular diseases, renal insufficiency, malignancy, and other medications, such as aspirin have been described as increasing the risk for bleeding \(^{164},^{165}\).
1.8 Post-stroke fatigue

1.8.1 Epidemiology and definition

Many patients suffer from fatigue after a stroke \(^{180-182}\). The fatigue is subjective and manifests as both physical and mental lack of energy. Many patients mention fatigue as one of the most difficult sequelae to which to adjust \(^{181}\). The fatigue often interferes with the rehabilitation process and impairs the ability to regain functions lost due to the stroke \(^{183}\). Post-stroke fatigue is so far a vague condition without an established definition. To study fatigue, it is necessary to try to define what aspect of fatigue is of interest. Staub et al. have described in an editorial the important distinctions between objective and subjective fatigue \(^{184}\). The subjective fatigue, a feeling of early exhaustion, is the aspect that is important for stroke survivors. Another useful distinction is between fatigability, fatigue that develops in connection with activities requiring sustained effort, and fatigue as a primary condition that is described as lack of initiative with imbalance between a preserved motivation and a decreased effectiveness. The same editorial suggests that post-stroke fatigue should be defined as “a reversible decrease or loss of abilities associated with heightened sensation of physical or mental strain, even without conspicuous effort, an overwhelming feeling of exhaustion, which leads to inability or difficulty to sustain even routine activities and which is commonly expressed verbally as a loss of drive” \(^{184}\).

Post-stroke fatigue is still a relatively unexplored condition. In other chronic diseases such as multiple sclerosis \(^{185}\), rheumatoid arthritis \(^{186, 187}\), and HIV \(^{188}\), fatigue is a common symptom and much more studied. Fatigue is also one of the most common symptoms among patients with cancer \(^{189, 190}\). The prevalence among stroke survivors is not well known. In a study performed by Ingels et al., 68% of stroke patients reported fatigue \(^{181}\). The occurrence of fatigue among 90 stroke patients was 51% as compared with 16% in age-matched controls \(^{180}\). Diffuse cerebral symptoms such as fatigue, impaired memory, inability to concentrate, emotional stability, and irritability have been shown to be present among 75% of patients 6-26 months after stroke. In a primary care setting, the prevalence of fatigue as a main complaint was 5-10%, with a normal distribution in severity \(^{191, 192}\).
1.8.2 Why does the stroke patient feel fatigued?

It has been hypothesised that fatigue after stroke results from a combination of organic brain lesion and psychosocial stress related to adjustment to a new life situation. Other clinical dysfunctions, such as sleep apnoea, may also cause fatigue after stroke.

Fatigue is a pivotal component of post-stroke depression. The condition is actually one of diagnostic criteria for depression. However, a patient can experience fatigue without other symptoms that are characteristic for depression, and this has been shown for Parkinson’s disease and for multiple sclerosis. In the study by Ingles et al, 39% of stroke patients experiencing fatigue were not classified as being depressed. Among those who were not depressed, fatigue was more common among stroke patients than among controls. Similar results were found in a study on fatigue and depression in stroke patients where 62% of stroke patients with fatigue did not have elevated depression scores. Fatigue accompanying post-stroke depression is often relieved when the depression is adequately treated.

It has previously been reported that post-stroke fatigue is not related to location. In a pilot study performed by Staub et al., fatigue correlated with lesion site but not with lesion side. They found a high frequency of lesions in the brainstem and a low frequency of cortical lesions among patients with fatigue. In accordance with this finding, the connection between the specific brain lesions and fatigue has been discussed in other diseases. Basal ganglia and impairment of striatal dopaminergic inputs have been associated with fatigue in patients with Parkinson’s disease. This is known to lower cortical activation and reduce voluntary attention.

1.8.3 Measurement of fatigue

When measuring fatigue, self-estimation scales are often used. Some scales are applicable for several types of fatigue and some scales measure fatigue caused by a specific disease. No scale has yet been developed specifically for post-stroke fatigue. When studying post-stroke fatigue, most studies use multidimensional questionnaires, estimating the self-perceived fatigue.
1.8.4 Treatment of post-stroke fatigue

Because the mechanism for post-stroke fatigue probably is multidimensional, there are several strategies for treatment. Patients with cause-specific fatigue, i.e., nutritional and metabolic deficiencies, anaemia, thyroid disease, diabetes, respiratory or cardiovascular disease, should be treated. Patient/family education is needed to reduce distress, to manage symptoms and to help to maintain a feeling of control when experiencing fatigue. In the literature there is a lack of intervention studies on post-stroke fatigue. What is known is interpolated from treatment studies of fatigue in association with other conditions and diseases. Several interventions have been tried for the chronic fatigue syndrome and in a review, behavioural therapy, as graded exercise therapy and cognitive behavioural therapy showed some positive effects. Similar results were shown for treatment with immunoglobulin and hydrocortisone. However, the suppressive effect of hydrocortisone on adrenal glands limits usage in routine practice. In studies of antidepressants, and especially for tricyclic antidepressants such as amitryptilin, it was shown that the beneficial effect may occur with lower doses than for treatment of depression. For chronic fatigue syndrome, serotonergic antidepressants are more effective for the pain component while chatecolaminergic agents are effective for symptoms associated with depression. According to what disease or condition the fatigue is associated with, there are different mechanisms causing fatigue and subsequently different therapies are needed.
The general objective was to study variations in stroke care in Sweden as reflected by Riks-Stroke, the Swedish national quality register for stroke care.

In more detail we aimed at performing studies on:

- The validity of Riks-Stroke, to ensure that data in the register were representative for patients with strokes in Sweden. The coverage, the case ascertainment, and the item validity of Riks-Stroke were to be assessed.

- Differences in management and outcome between patient groups, in particular with focus on sex differences.

- Verification in routine clinical practice of beneficial effects of interventions studied in controlled randomised studies. More specifically, we aimed at studying long-term effects of stroke unit care as compared with care in general wards.

- Variations in management between hospitals, counties and health care regions. For example, a study of variations in usage of oral anticoagulants as stroke prevention in stroke patients with atrial fibrillation.

- Long-term consequences of stroke and their impact on outcome. Post-stroke fatigue is a relatively unexplored condition after stroke and we aimed at studying prevalence, predictors and outcome.
3 PATIENTS AND METHODS

3.1 The Riks-Stroke register

Riks-Stroke, the Swedish national quality register for stroke care, was established in 1994 and from 1998 the register covers all hospitals in Sweden admitting patients with acute stroke. However, in some hospitals, the register is still in a build-up phase and the coverage of stroke is incomplete. The present thesis is based on data from 1996 to 2001. As shown in Figure 2, the number of stroke events included in RS during these years has increased from 14,308 to 20,910 per year.

![Graph showing number of stroke events, reporting hospitals, and coverage from 1995 to 2001.]

Figure 2. Number of reporting hospitals, number of stroke events and coverage according to epidemiological estimates in Riks-Stroke.

Information from before the stroke and about treatment in hospital is collected during the hospital admission. Three months after the stroke, the patient is contacted by mail or by telephone and asked to fill in a questionnaire. A computerised data registration sheet is used and local data on acute treatment and three-month follow-up are submitted by an Internet-based system to the national data management centre of RS. Once a year, each participating hospital receives feed-back information. The results from each hospital are compared with the summarised national data.
Valid stroke diagnoses in RS are cerebral infarction, intracerebral haemorrhage and unspecified stroke (ICD-10; I61, I63 and I64). In addition, all recurrent stroke events must occur at least 28 days after the first stroke. Inclusion of TIAs and subarachnoid haemorrhage (SAH) is optional, but they are not summarised in national reports or in this thesis.

The strategy of RS is to prioritise coverage over details. Thus, data collection is kept very simple. Nevertheless, RS is a dynamic register that is constantly adjusted to changes in routine health care. In the past decades, focus on stroke research and stroke care has increased. With a more complex stroke care, the requirements for information needed for evaluation also increase. As a consequence of this, data collection in RS has gradually increased and today the register includes items on background, process, structure and outcome (Appendix 1).

3.2 Two-year follow-up performed in 1999

The two-year follow-up of stroke patients was performed within the framework of a project to map the life situation of elderly people in Sweden, "Äldreuppdraget" [The Elderly Project], commissioned by the government for the National Board of Health and Welfare. The aim of this follow-up was to survey the life situation of stroke patients two years after the stroke. RS performed the follow-up in co-operation with the National Board of Health and Welfare.

During the first six months of 1997, 8,194 patients had an acute stroke event that was registered in RS. In October 1999, a follow-up by mail questionnaire was performed on these patients. The average follow-up time was 30.4 months (SD 1.7). To identify those patients who had died between the three-month and the two-year follow-up, RS data were linked to national mortality data. The number of patients who had died was 3,005 of 8,194 (36.7%) and 5,189 patients were still alive.

A new questionnaire was constructed for the follow-up two years after the stroke. It was based on the same questions as in the three-month follow-up within the RS program. Items included are shown in Table 4. The single-question approach for assessing stroke outcome and need of help has been shown to be well suited for large epidemiological studies. The follow-up questionnaire was sent by mail to 5,104 patients. The other 85 patients were still alive but their current mailing addresses were not found. The patients received one reminder to answer the questionnaire. When the data collection phase was finished, 4,038 had sent back the questionnaire (78.8%) and fifteen patients were not
included in the analyses because their identification numbers had been lost. Approximately half of the patients (52.9%) had completed the questionnaire by themselves. In 22.4% it was completed by a next-of-kin alone, and in another 24.8% it was completed with the help of health care personnel or someone else.

**Table 4. Items included in the two-year follow-up questionnaire in 1999.**

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Age</th>
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<tbody>
<tr>
<td></td>
<td>Sex</td>
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<tr>
<td>Living situation</td>
<td>Type of living</td>
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<td></td>
<td>Co-habitant status</td>
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<td>Dependency in primary ADL</td>
<td>Mobility</td>
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<td>Toileting</td>
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<td></td>
<td>Dressing</td>
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<td></td>
<td>Eating/drinking</td>
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<td>Personal hygiene</td>
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<tr>
<td>Dependency in secondary ADL</td>
<td>Preparation of food</td>
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<td>Grocery shopping</td>
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<td>Self-perceived health</td>
<td>General health</td>
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<td>Depression</td>
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<td></td>
<td>Fatigue</td>
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<td></td>
<td>Pain</td>
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<tr>
<td>Cognitive impairments</td>
<td>Speaking</td>
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<td>Reading</td>
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<td></td>
<td>Writing</td>
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<tr>
<td>Need of/satisfaction with help or support</td>
<td>From health care and municipal care</td>
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<td></td>
<td>From informal caregivers</td>
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<td></td>
<td>Knowledge about who to contact to receive more help</td>
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<tr>
<td>Performance of interests from before the stroke</td>
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</tbody>
</table>
3.3 Validation of Riks-Stroke

3.3.1 Case validity

Coverage

This study estimated the proportion of the “definite” stroke population that is treated in hospitals in Sweden that is included in RS.

Comparison with National Discharge Register (NDR). From NDR we obtained all hospital admissions in hospitals reporting to RS during 1998-2001 with one of the ICD-10 stroke diagnosis I61, I63 or I64. If a patient had a new hospital admission with a stroke diagnosis within 28 days after first day of the first admission, the second was excluded. These hospital admissions in NDR were compared with stroke events reported to RS during the same period of time and the proportion included in both registers was calculated.

Epidemiological estimates. The estimation of stroke events in Sweden is difficult to perform because most studies measure stroke incidence and not both first-ever and recurrent stroke events. The total annual incidence of stroke in Sweden has been shown to range between 290 and 315 per 100,000 inhabitants \(^{13, 14, 212, 213}\). Based upon a population of 9 million, the number of first-ever stroke events each year in Sweden should range from 26,000 to 28,350. In the RS register, 28% of all stroke events are recurrent strokes. This figure agrees well with findings in previous studies \(^{3, 4, 8}\). The estimated number of all stroke events of 300 per 100,000 used in epidemiological evaluations of RS is probably an underestimation, but allows for regional variations in stroke occurrence.

Case ascertainment

This study is a comparison between characteristics of patients with stroke events that were included in RS and patients with stroke events that were not included in RS. During the first six months of 1998, a total of 9,388 stroke events from 84 hospitals/hospital clusters in Sweden were entered into the database. For this study, we randomly selected 20 hospitals (2 university hospitals, 8 middle-sized county hospitals and 10 small district hospitals). In these hospitals we randomised 15 stroke events included in RS. From NDR, stroke events that were not included in RS during the same period were identified and
20 at each hospital were randomised. The study population is shown in Figure 3.

Patients included in RS during first six months of 1998
84 hospitals, N=9,388

Random selection of 20 hospitals

2 university hospitals 8 county hospitals 10 district hospitals

Random selection at each hospital of 20 patients included in only NDR
N=400

Random selection at each hospital of 15 patients included in NDR and in RS, N=700

Total stroke population N=700

98 Patients records not included

For 56 stroke events the hospital records were missing.

For 13 stroke events the acute phase care and the rehabilitation care were randomised as separate events but in our analyses they were included as the same event.

29 stroke events were identified as not included in RS but the RS questionnaire for the acute phase had been completed and included in the hospital chart but not submitted to the national RS database.

309 patients in NDR but not in RS 293 patients in NDR and in RS

Figure 3. Study population in the validation study of case ascertainment in Riks-Stroke (RS) as compared with the National Discharge Register (NDR) and hospital records.
Hospital records from the stroke event of interest were requested from participating hospitals and abstracted. We included information about sex, age, history of previous stroke, co-morbidities (AF, diabetes, hypertension, smoking, previous myocardial infarction, cardiac failure), use of pre-selected antithrombotic medications before stroke, living condition and need of assistance in primary ADL functions. Level of consciousness, right- or left-sided paresis and if the patient was already treated in hospital at stroke onset were recorded. Items related to acute care included type of department (medical, neurological, geriatric, etc.), treatment in organised stroke care (stroke unit), CT scan performed and antithrombotic drug treatment during the acute phase. At discharge, length of acute care hospital stay, status at discharge (dead or alive), dependency in primary ADL function, further management (at home, in institutions at various levels) and antithrombotic medications (both already begun and planned) were recorded.

In this study we classified stroke diagnosis in RS and in hospital discharge register as definite stroke events (according to validation criteria; stroke according to WHO criteria and recurrent strokes within 28 days are not considered as new stroke events), uncertain stroke events (clinical signs indistinctly reported in medical record or not in agreement with validation criteria) or not stroke (obviously not treated for a new stroke event). For those patients who were treated in hospital with a stroke diagnosis, but did not fulfil the validation criteria for a stroke event, the reason for discrepancy was recorded.

3.3.2 Item validity

Accuracy of data

This study measured the accuracy of data in the database. It was performed by a comparison between data in hospital records and data in the RS database. The study was based on 14,308 stroke events reported to RS in 1996. We selected seven hospitals from the RS register with the best coverage of stroke events according to epidemiological estimates. The selected hospitals represented different levels of hospital care; four small district hospitals, two middle-sized county hospitals and one university hospital. For inclusion in the study we randomly selected 395 stroke events reported to RS in these hospitals.

Information about the 395 stroke events was collected in a retrospective study of the hospital records and compared to information reported to RS. Items studied in the RS form for acute care were need of assistance in primary ADL (mobility, toilet visits and dressing), previous
stroke, level of consciousness on admission, CT scan performed, day for stroke onset, day of admission, day of discharge. Also the information about wards and clinics in which the stroke care was performed and to where the patient was discharged was validated. One physician together with a research assistant performed this data collection and the conformity was tested on 50 hospital records before the study was started. Hospital records were missing for 24 stroke events leaving 371 stroke events for inclusion in the analyses.

**Validation of RS forms**

The criterion validity of questions used in the RS form was tested against well established instruments in concerned areas. The study population in this study was based on patients treated for stroke at the Stroke Centre of the University Hospital in Umeå during 2002 and who were reported to RS. The study population consisted of 36 patients. A stroke nurse contacted the patients and a personal interview was performed approximately 3 months after the stroke. The patients were strategically chosen to represent different levels of functional impairment, according to the Barthel index, at the time for the interview. Thirteen patients had Barthel index below 60, 10 patients had scores in the interval 60-89 and 13 patients had scores above 90.

The Barthel index was completed to assure that the study group represented different levels of functional impairment and to validate ADL questions in the RS three-month follow-up form. ADL in RS was assessed by mobility, dependence of help for toilet visits, for dressing/undressing, and by a summary measure of ADL (dependent ADL: not fully mobile and/or needed help with toilet visits and/or needed help with dressing/undressing). Each separate ADL question and the summary measure were validated by comparisons with the sum of the Barthel ADL index. Fatigue was compared with the mean Brief Fatigue Inventory (BFI).
3.4 Other specific methods

3.4.1 Data from Riks-Stroke database (Papers I and III)

These cross sectional cohort studies were based on data from 2001. During this year, a total of 20,761 patients from 84 hospitals/hospital clusters in Sweden were entered into the database. Based on estimates from epidemiological data and official discharge registries, the coverage rate of each hospital was assessed. Nine hospitals that reported less than 70% of the expected number of stroke patients were excluded leaving 19,547 patients in 75 hospitals. These patients were included in analyses on gender differences. At the three-month follow-up, 3,333 patients had died and 13,397 patients had completed a three-month follow-up questionnaire. Information from the three-month follow-up was missing for 2,817 patients and they were excluded from analyses of follow-up data.

In these 75 hospitals, information about treatment with anticoagulants or information about AF was missing in 726 patients (3.7%) and these patients were excluded from further analyses on treatment with OA in Paper III. A diagnosis of ischaemic stroke was accepted only if a CT scan or the autopsy had excluded an intracranial bleeding. CT scan was performed in 96.4% of patients included in the study. Those patients who had not been examined by CT or were deceased and had not had an autopsy were also removed from analyses, leaving 18,276 patients for analyses of AF and OA. AF was diagnosed if the present ECG showed AF or atrial flutter on admission to hospital or if the patient had a previous diagnosis of AF.

3.4.2 Data from two-year follow-up (Papers II and IV)

These prospective cohort studies were based on the 8,194 patients included in RS during first six months of 1997 and who were subjects for follow-up two years after stroke. A total of 5,134 patients (62.7%) were treated in SUs and 2,400 (29.3%) were treated in GWs. Those 659 (8.0%) patients who were treated in a setting which neither fulfilled the criteria for a SU nor a GW, together with one patient for whom information about type of acute care was missing, were excluded from further analyses leaving 7,534 patients for analyses of long-term effects of SU care in Paper II.

Fatigue is often a part of a depression and as shown in Table 5, there was a statistically significant relationship between feelings of
tiredness and feelings of depression. Therefore, those 153 patients who reported that they always felt depressed and the 65 patients who did not answer the question “do you feel depressed?” were excluded from further analyses on post-stroke fatigue in Paper IV, leaving 3,667 patients. On the question “do you feel tired?” there were four possible answers to chose between: never tired, seldom tired, often tired or always tired. Patients were divided into three categories. Those patients who were never or seldom felt tired were classified as not being fatigued, those patients who were often tired were classified as having a moderate fatigued and those patients who were always tired as having a severe fatigue.

Table 5. Relationship between feelings of tiredness and feelings of depression in the two-year follow-up study.

<table>
<thead>
<tr>
<th></th>
<th>Never depressed</th>
<th>Sometimes depressed</th>
<th>Often depressed</th>
<th>Always depressed</th>
<th>Total Tota</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Never tired</td>
<td>337</td>
<td>27.7</td>
<td>63</td>
<td>3.3</td>
<td>2</td>
</tr>
<tr>
<td>Sometimes tired</td>
<td>692</td>
<td>57.0</td>
<td>1064</td>
<td>55.9</td>
<td>73</td>
</tr>
<tr>
<td>Often tired</td>
<td>151</td>
<td>13.7</td>
<td>622</td>
<td>32.7</td>
<td>297</td>
</tr>
<tr>
<td>Always tired</td>
<td>35</td>
<td>2.9</td>
<td>156</td>
<td>8.2</td>
<td>175</td>
</tr>
<tr>
<td>Total</td>
<td>1215</td>
<td>1905</td>
<td>547</td>
<td>153</td>
<td>3820</td>
</tr>
</tbody>
</table>

\( \chi^2 = 1684, p < 0.001 \)

3.5 Consent

All acute stroke patients admitted to hospitals in Sweden and who are included in RS are informed about the registration in RS. If they do not agree to being included they are removed from the database. The RS has been approved by the Research Ethics Committee of Umeå University and the data-handling procedures by the National Computer Data Inspection Board. For the two-year follow-up study, a specific approval has been received from the Research Ethics Committee of Umeå University.
3.6 Statistical analyses

3.6.1 General

Statistical analyses were performed with the SPSS statistical package (version 10.0)\textsuperscript{216}. Comparisons in mean age between groups were performed with Student’s t-test. Testing for significance of differences for category variables were performed with $\chi^2$-test. Age-adjusted analyses of category variables were performed by binary logistic regression with age as a co-variable.

Multiple logistic regression analyses were performed to adjust for differences in background variables at the time of the stroke event, at the three-month follow-up or at the two-year follow-up. They were also used for identification of independent predictors for the outcome of interest. Conditions/variables that were considered to be potential prognostic factors were included in the analyses and are presented for each Paper in Table 6. Each background variable was first tested separately, adjusted for age, and then analysed with a multiple stepwise backward design. The models were also tested with a manual removal of variables (by their known clinical importance) and with a stepwise forward design. These selection procedures resulted in the same final models as the backward procedures, hence not changing the odds ratios or confidence intervals. The stepwise method systematically removed variables that were not statistically significant, leaving a final model. Odds ratios are presented with corresponding 95% confidence intervals.

3.6.2 Validation of Riks-Stroke

In the study on case ascertainment, comparisons between patients included in RS and patients not included in RS were presented as proportions with 95% confidence intervals. In the study assessing accuracy of data in the database by comparing RS data with hospital records, age and length of stay at hospital were analysed as linear variables, and comparisons between groups were performed with Student’s t-test. Item validity was described as proportion with agreement between hospital record and RS data at each individual hospital. Distributions between hospitals in item validity were described as medians with a range between highest and lowest values.
Table 6. Variables included in multiple logistic regression analyses (Papers I-IV).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Paper I Type of Living</th>
<th>Paper II ADL</th>
<th>Paper II Case fatality</th>
<th>Paper III 1&lt;sup&gt;st&lt;/sup&gt; Prevention</th>
<th>Paper III 2&lt;sup&gt;nd&lt;/sup&gt; Prevention</th>
<th>Paper IV ADL</th>
<th>Paper IV Case fatality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At stroke onset and during acute care</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, linear</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Age, categories</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Sex</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Co-habitant status</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Type of living ADL function</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>First-ever/ recurrent stroke</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Diabetes</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Hypertension</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Conscious/ unconscious on admission</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Treatment in SU/GW Examination with CT scan</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Health care region</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of living at discharge</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>At three-month follow-up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADL-function</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Self-perceived general health</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Feeling of Depression</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>At two-year follow-up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Co-habitant status</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Speech impairments</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Self-perceived general health</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Feeling of depression</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
The association between questions in the validation of RS forms was presented using box- and/or scatter-plots. The concurrent validity was assessed by Spearmans’s rank correlation coefficient, $r_s$ (ranging from -1 to 1). A high absolute value of $r_s$ implies a high level of agreement and is therefore also a measure of validity.

### 3.6.3 Individual studies

#### Paper I

Comparisons between men and women were adjusted for age because women were on average, 4.5 years older when they had their stroke. The variables regarding pre-stroke status and acute stroke care included in the multiple logistic regression models for adjustment of differences in background variables and for prediction of institutional living at three-month follow-up are shown in Table 6. Because of a high frequency of missing values for the self-estimated health variables, the missing values were categorised into a third category and included in the analyses. The frequency of missing values for other variables was less than 10% and patients with missing values were excluded in the regression models.

#### Paper II

Comparisons between patients treated in SUs and patients treated in GWs were adjusted for age, because the patients treated in GWs were on average 1.4 years older when they had their stroke. Multiple logistic regression analyses were performed to adjust for differences in case mix at the time of the stroke event and included variables are shown in Table 6. The frequency of missing values was less than 10% for each variable and patients with missing values were excluded in the regression models. The same strategy was used for modelling survival, using the Cox proportional hazard model.

#### Paper III

Between-hospital analyses were performed on hospitals that treated 40 AF patients or more. All other analyses were based on the total RS sample included in this study. All comparisons between categories in proportion treated with OA were adjusted for age.

Multiple logistic regression analyses were performed to adjust for differences in background variables seen at the time of the stroke event and to identify independent predictors of anticoagulant treatment. Variables included in multiple analyses are shown in Table 6. The
frequency of missing values was less than 10% for each variable and patients with missing values were excluded in the regression models.

Not all continuous variables were normally distributed and Spearman’s rank correlation coefficient was used for correlation analyses at hospital level.

**Paper IV**

Multiple logistic regression analyses were performed to adjust for differences in background variables seen at the time for the stroke event. All variables from before the stroke and during the acute care were considered to be potential prognostic factors and were included in the analyses. The variables included in the regression models are shown in Table 6. The same strategy was used for modelling survival one year after the two-year follow-up, using the Cox proportional hazard model. Even in models where age was not a significant predictor for the outcome, age was included in the final models to adjust the results for age differences. Patients with missing values were less than or approximately 10% and they were excluded in the logistic regression models. In the Cox proportional hazard model, missing values were first included in the models as a category on its own, belonging to a categorical variable. However, they were only included in the final model if they affected the results in a statistically significant manner.
4 RESULTS

4.1 Validity of the Riks-Stroke register

4.1.1 Case validity

Coverage

Comparison with National Discharge Register (NDR). Approximately half of the hospital admissions with stroke diagnoses in NDR occurred in RS as well. Table 7 shows that the proportion ranged from 47.5% in 1998 to 55.1% in 2001. This rise in coverage according to the NDR was mainly due to a gradual decrease of hospital admissions with stroke diagnoses in NDR. In the study of case ascertainment in RS presented below, 73% of the patients in NDR were considered “definite strokes” according to the validation criteria. When recalculating coverage of RS data compared to definite strokes in NDR, the proportion that occurred in both registers ranged from 65.1% to 75.5%. The proportion included only in RS and not in NDR decreased but represented only 2.6% in 1998 and 2.1% in 2001.

Epidemiological estimates. As shown in Figure 2, the number of stroke events reported to RS has increased from 19238 in 1998 to 20910 in 2001 and from 1998 all 84 hospitals/hospital clusters that treat acute stroke report to RS.

Table 7. Number of stroke events included in both National Discharge Register (NDR) and Riks-Stroke (RS), only in NDR and only in RS.

<table>
<thead>
<tr>
<th>Year</th>
<th>Pooled data from RS and NDR</th>
<th>RS and NDR</th>
<th>NDR only</th>
<th>RS only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>1998</td>
<td>38,184</td>
<td>18,146</td>
<td>47.5</td>
<td>19,054</td>
</tr>
<tr>
<td>1999</td>
<td>37,171</td>
<td>19,545</td>
<td>52.6</td>
<td>16,727</td>
</tr>
<tr>
<td>2000</td>
<td>36,204</td>
<td>19,097</td>
<td>52.7</td>
<td>16,325</td>
</tr>
<tr>
<td>2001</td>
<td>34,747</td>
<td>19,138</td>
<td>55.1</td>
<td>14,890</td>
</tr>
</tbody>
</table>
Figure 4. Comparison between coverage according to National Discharge Register and according to epidemiological estimates

Table 8. Case ascertainment. All stroke events included in both National Discharge Register (NDR) and Riks-Stroke (RS) were compared with stroke events included only in NDR and only in RS.

<table>
<thead>
<tr>
<th></th>
<th>RS &amp; NDR</th>
<th>NDR only</th>
<th>RS only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke as main diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>96</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>96</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>96</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>95</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>51</td>
<td>50</td>
<td>56</td>
</tr>
<tr>
<td>1999</td>
<td>51</td>
<td>49</td>
<td>52</td>
</tr>
<tr>
<td>2000</td>
<td>50</td>
<td>49</td>
<td>50</td>
</tr>
<tr>
<td>2001</td>
<td>50</td>
<td>50</td>
<td>53</td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>60</td>
<td>63</td>
<td>58</td>
</tr>
<tr>
<td>1999</td>
<td>60</td>
<td>63</td>
<td>57</td>
</tr>
<tr>
<td>2000</td>
<td>62</td>
<td>62</td>
<td>57</td>
</tr>
<tr>
<td>2001</td>
<td>62</td>
<td>63</td>
<td>62</td>
</tr>
<tr>
<td>Proportion living at home before stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>98</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>98</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>97</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>94</td>
<td>93</td>
<td></td>
</tr>
</tbody>
</table>

The coverage of reported patients compared to estimated stroke events in Sweden has consequently increased from 71.3% to 77.4%. Correlation between coverage according to NDR and according to epidemiological estimates. When analysing data from 2001 on the hospital level, the previously mentioned methods for estimation of coverage of RS correlated well ($r_s=0.76; p<0.001$; Figure 4).

Case ascertainment

Comparison with National Discharge Register (NDR). Table 8 shows that stroke diagnoses were more often registered as main diagnoses in RS than in NDR. There was a tendency towards patients only in NDR being older than patients included in both NDR and RS, although this difference diminished until 2001. Among patients in only NDR and among patients in both
Table 9. Validation of diagnosis in Riks-Stroke (RS) and National Discharge Register (NDR) according to RS criteria.

<table>
<thead>
<tr>
<th></th>
<th>Definite strokes n</th>
<th>Uncertain strokes n</th>
<th>Unlikely strokes n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>RS and NDR</td>
<td>278 94.9</td>
<td>11 3.8</td>
<td>4 1.4</td>
</tr>
<tr>
<td>NDR only</td>
<td>226 73.1</td>
<td>28 9.0</td>
<td>55 17.8</td>
</tr>
</tbody>
</table>

Table 10. Reasons for validating stroke diagnosis in Riks-Stroke (RS) and National Discharge Register (NDR) as uncertain or unlikely stroke events.

<table>
<thead>
<tr>
<th></th>
<th>RS and NDR</th>
<th>NDR only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Uncertain stroke</td>
<td>Unlikely stroke</td>
</tr>
<tr>
<td></td>
<td>N=11</td>
<td>N=4</td>
</tr>
<tr>
<td>Non-focal</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>Non-focal</td>
<td>symptoms</td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Unconscious at</td>
<td></td>
<td></td>
</tr>
<tr>
<td>onset</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Post stroke status</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Misprint</td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

NDR and RS, the proportion of patients living at home before stroke has decreased.

Comparison with hospital records. As shown in Table 9, a definite stroke diagnosis according to validation criteria was found in 94.9% of the RS patients and in 73.1% among those patients not included in RS. An uncertain stroke or an unlikely stroke according to the validation criteria, were more common in the group of patients not included in RS.

Of those patients who received an unlikely stroke diagnosis according to the validation criteria, 40 out of 59 had previously been treated for stroke as an inpatient and received a new stroke diagnosis without suffering a new stroke event during the current hospital admission (Table 10).

In Table 11, those patients with a definite stroke according to validation criteria among RS patients are compared with patients with a definite stroke diagnosis who were not included in RS. There were no statistically significant differences between the groups beside patients not included in RS were more often already treated as inpatients at stroke onset and less often treated in SUs. There were tendencies towards a higher proportion of patients in RS being 75 years or older (mean age 76.5 years vs. 75.7 years; p=0.51) and a lower proportion of women
being included in RS. The RS patients were more often independent in primary ADL and living at home before stroke. On admission there were no differences in stroke subtype, level of consciousness or side of paresis. Patients included in RS had an apparent lower case fatality rate than those not included and this was true both for 7-day and 30-day case fatality rates, but the differences did not reach statistical significance.

Table 11. Validation of cases in Riks-Stroke (RS). Comparison between definite strokes included in National Discharge Register (NDR) and RS and definite strokes included only in NDR.

<table>
<thead>
<tr>
<th></th>
<th>Riks-Stroke</th>
<th>Not in Riks-Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N= 278</td>
<td>N= 226</td>
</tr>
<tr>
<td><strong>Before stroke</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>178</td>
<td>226</td>
</tr>
<tr>
<td>Men</td>
<td>278</td>
<td>226</td>
</tr>
<tr>
<td>Independent primary ADL</td>
<td>244</td>
<td>187</td>
</tr>
<tr>
<td>function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living at home</td>
<td>274</td>
<td>214</td>
</tr>
<tr>
<td>Living alone</td>
<td>257</td>
<td>203</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent stroke</td>
<td>273</td>
<td>216</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>269</td>
<td>211</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>270</td>
<td>216</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>270</td>
<td>221</td>
</tr>
<tr>
<td>Hypertension</td>
<td>268</td>
<td>212</td>
</tr>
<tr>
<td>Diabetes</td>
<td>273</td>
<td>220</td>
</tr>
<tr>
<td><strong>At stroke onset</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracerebral haemorrhage</td>
<td>278</td>
<td>226</td>
</tr>
<tr>
<td>Fully conscious on admission</td>
<td>256</td>
<td>197</td>
</tr>
<tr>
<td>Right-sided pareses</td>
<td>220</td>
<td>169</td>
</tr>
<tr>
<td><strong>During stroke care</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT scan</td>
<td>278</td>
<td>222</td>
</tr>
<tr>
<td>In-hospital care at stroke onset</td>
<td>277</td>
<td>224</td>
</tr>
<tr>
<td>SU care</td>
<td>270</td>
<td>217</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent primary ADL at discharge</td>
<td>201</td>
<td>151</td>
</tr>
<tr>
<td>7-d case fatality</td>
<td>273</td>
<td>218</td>
</tr>
<tr>
<td>30-d case fatality</td>
<td>276</td>
<td>220</td>
</tr>
</tbody>
</table>

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4.1.2 Item validity

Accuracy of data

There was a 94% agreement between stroke diagnoses in RS and in patient records. The variation between hospitals ranged from 87.5% to 98.1%. In those hospitals with lower agreement on stroke diagnoses, unspecified stroke was often recorded instead of cerebral infarction. As shown in Figure 5, items in RS measuring need of help for primary ADL, examination with CT scan, and day for discharge from hospital had a good concordance in comparison with information in hospital records. Living situation, co-habitant status, first-ever/recurrent stroke, day for admission to hospital, and SU or GW care had a concordance of 90% or more. This information was also often recorded clearly in the patient records and easy to assess during validation study making the comparisons accurate and trustworthy. Information on SU or GW care showed a large variation between the hospital with highest agreement and hospitals with lowest agreement. As an example, in one hospital there were uncertainties as to whether they had an organised SU care or not, and patients treated in the same ward were recorded differently in RS. In another hospital they had decided on a local variant to register type of ward.

![Figure 5. Item validity. Median concordance in per cent between information in Riks-Stroke and in hospital records. Lines show range from highest to lowest value of concordance for the variable in the individual hospitals.](image_url)
Level of consciousness, to where the patient was discharged, and day of onset had a concordance of less than 90%. Information on level of consciousness was often missing in hospital records, and when the information was present it was not easily assessable because an established scale as RLS was often not used. Instead the level of consciousness was expressed vaguely making it difficult to evaluate this information.

Validation of RS forms

ADL in RS forms vs. Barthel ADL index. The ADL questions concerning mobility, help with toilet, help with dressing, and the summary measure showed a strong correlation with Barthel index, \( r_s = -0.86, -0.74, -0.83, -0.80 \) respectively (all \( p<0.001 \)), thereby confirming concurrent validity. As seen in Figure 6, the categories were nicely separated with respect to Barthel index. All but one of the 13 patients with Barthel scores 90 or above were correctly classified as ADL independent using the RS ADL summary measure. Of the 23 patients who had Barthel scores < 90, two patients with scores 75 and 80 had been misclassified as ADL independent (sensitivity 92% and specificity 91%). Hence, the summary ADL measure has a good ability to discriminate between ADL-dependent and ADL-independent patients as determined by Barthel scores over/under 90.

Figure 6. Categorisation of ADL function into independent/ dependent according to Riks-Stroke questionnaire, plotted against Barthel index. The box represents the inter-quartile range and the line within the box represents the median. The whiskers extend to the lowest and the highest values having outliers that are marked with circles.

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Fatigue vs. the mean Brief Fatigue Inventory scale (BFI). The RS fatigue question correlated reasonably well with mean BFI, $r_s=0.65$ ($p<0.001$). The variation within fatigue categories was large with respect to mean BFI resulting in overlapping categories. However, the question discriminated well between never/sometimes fatigue and often/always fatigue (Figure 7). When patients with mean BFI $\geq 7$ are diagnosed with fatigue, all 4 patients classified as fatigued were correctly classified using the RS classification. Of the 32 patients who were not fatigued using BFI, 8 were misclassified (sensitivity 100% and specificity 75%. NB! Estimations were based on very few patients).

![Fatigue vs. BFI](image)

**Figure 7.** Categorisation of fatigue according to Riks-Stroke questionnaire and plotted against fatigue according to mean Brief Fatigue Inventory. For interpretation of the box-plot, see legend to Figure 6.
4.2 Management of stroke

4.2.1 Sex differences in management and outcome after stroke

**Before the stroke and during in-hospital care**

Of the 19,547 patients included in the study, 9,881 (50.5%) were men and 9,666 (49.5%) were women. The mean age was 75.5 years, women being 4.5 years older than men (77.8 vs. 73.2 years; \( p<0.001 \)). Even after adjustment for age, women were more frequently living at home with community support or in an institution before the stroke, while men were more often living at home without help from the community. Among those living at home, women were more often living alone. Women were also more dependent upon help with their daily activities. Recurrent stroke, diabetes and smoking were more common among men while more women had a diagnosis of hypertension or were on hypertensive treatment.

On arrival to hospital, impaired consciousness was slightly more frequent among women than men. Equally many women and men underwent CT scan and treatment in an SU. On admission to hospital, female patients with first-ever stroke were, also after age-adjustment, less often treated with antithrombotic agents. For patients with AF, women were less frequently treated with OA on admission. At discharge from hospital, women received antithrombotic agents as secondary stroke prevention less often than men. Women with AF were also less often treated with OA but more often treated with antiplatelet agents as secondary prevention.

**Three-month follow-up**

The 7-day, 28-day or 90-day case fatality rates did not differ between men and women. Among patients who had been living at home before stroke, more women changed their residency to an institution. Fewer women were living together with a close relative and this was also true for patients still living at home. More women needed help with primary ADL.
Table 12. Separate and multiple analyses of institutional living at three-month follow-up, among patients who lived at home before stroke. Riks-Stroke data 2001 (Paper I).

<table>
<thead>
<tr>
<th></th>
<th>Separate analyses (age adjusted)</th>
<th>Multiple analyses</th>
<th>N=11,661</th>
<th>N=11,041</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;84</td>
<td>Reference category</td>
<td>Reference category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75-84</td>
<td>0.43</td>
<td>0.38 - 0.48</td>
<td>0.62</td>
<td>0.53 - 0.73</td>
</tr>
<tr>
<td>65-74</td>
<td>0.17</td>
<td>0.15 - 0.20</td>
<td>0.36</td>
<td>0.29 - 0.44</td>
</tr>
<tr>
<td>&lt;65</td>
<td>0.06</td>
<td>0.04 - 0.08</td>
<td>0.15</td>
<td>0.11 - 0.21</td>
</tr>
<tr>
<td>Women</td>
<td>1.37</td>
<td>1.23 - 1.53</td>
<td>1.18</td>
<td>1.01 - 1.38</td>
</tr>
<tr>
<td>Recurrent stroke</td>
<td>1.37</td>
<td>1.23 - 1.54</td>
<td>Rejected</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.57</td>
<td>1.39 - 1.79</td>
<td>1.34</td>
<td>1.14 - 1.56</td>
</tr>
<tr>
<td>Intracerebral haemorrhage</td>
<td>1.84</td>
<td>1.55 - 2.18</td>
<td>1.27</td>
<td>1.02 - 1.58</td>
</tr>
<tr>
<td>Fully conscious on admission</td>
<td>0.19</td>
<td>0.16 - 0.22</td>
<td>0.32</td>
<td>0.27 - 0.38</td>
</tr>
<tr>
<td>Stroke unit care</td>
<td>0.96</td>
<td>0.85 - 1.06</td>
<td>0.83</td>
<td>0.72 - 0.97</td>
</tr>
<tr>
<td>Living alone before stroke</td>
<td>1.80</td>
<td>1.61 - 2.01</td>
<td>2.28</td>
<td>2.28 - 3.05</td>
</tr>
<tr>
<td>Independent primary ADL at follow up</td>
<td>0.05</td>
<td>0.04 - 0.06</td>
<td>0.06</td>
<td>0.05 - 0.07</td>
</tr>
<tr>
<td>Self-estimated health at follow-up</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good/fairly good health</td>
<td>Reference category</td>
<td>Reference category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fairly bad /very bad health</td>
<td>3.51</td>
<td>3.07 - 4.00</td>
<td>1.45</td>
<td>1.22 - 1.72</td>
</tr>
<tr>
<td>Information missing</td>
<td>5.44</td>
<td>4.72 - 6.27</td>
<td>2.42</td>
<td>1.93 - 3.05</td>
</tr>
<tr>
<td>Feeling of depression at follow up</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never/sometimes feeling depressed</td>
<td>Reference category</td>
<td>Reference category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Often/Always feeling depressed</td>
<td>2.54</td>
<td>2.18 - 2.95</td>
<td>1.19</td>
<td>0.99 - 1.45</td>
</tr>
<tr>
<td>Information missing</td>
<td>4.07</td>
<td>3.53 - 4.70</td>
<td>1.88</td>
<td>1.47 - 2.39</td>
</tr>
</tbody>
</table>

A depressive mood was more common among women and the women more often estimated their general health as fairly bad or very bad. Women received more help from social and medical services. Among those who had not received help, more women than men expressed that they would have wanted help. Women were also more
dependent upon help and support from relatives. In total, women both wished to have more help and received more help than men.

As shown in Table 12, female sex predicted, also after adjustment for other factors, institutional living three months after stroke among patients who lived at home before stroke. Other independent predictors were high age, living alone at stroke onset, presence of diabetes, impaired consciousness on admission, not receiving care in SU, being dependent in primary ADL at follow up, estimating health as fairly bad or very bad and often or always feeling depressed.

### 4.2.2 Long-term effect of stroke unit care

#### Patient characteristics on admission and at three-month follow-up

Of the 7,534 patients included in the analyses, 5,134 (68.1%) were treated in SUs and 2,400 (31.9%) in GWs. Among patients who were independent in primary ADL functions before the stroke, 69.2% were treated in SUs, and among those dependent upon help for ADL before the strokes, 63.2% were treated in SUs (OR 1.27, CI 1.12-1.24).

**Patients independent in primary ADL functions before the stroke.** Patients treated in SUs were on average two years younger than those patients treated in GWs (73.5 vs. 75.5 years, p<0.001). Patients in the GW group had more often a cerebral haemorrhage and an impaired consciousness. After three months, more patients treated in GWs had died. Among those still alive, more patients treated in SUs were living at home and they were also more often independent in ADL functions.

**Patients dependent in primary ADL functions before the stroke.** There was no difference in age between patients treated in SUs and patients treated in GWs (80.4 respectively 80.0 years, p=0.43). The GW patients had more often a cerebral haemorrhage and an impaired consciousness at arrival to the hospital. Three months after the stroke more patients treated in GWs had died, but the difference was not statistically significant.

#### Two-year follow-up

**Case fatality rates.** A total of 1,721 patients of the 5,134 patients (30.2%) that had been treated in SUs for their strokes, had died at the time for the two-year follow-up. Among patients treated in GWs, 972 out of 2,400 (34.0%) had died, and they had, after age-adjustment, a significantly increased risk of dying within two years after stroke (OR 1.23, CI 1.15-1.33) as compared with patients in the SU group. The NNT for avoiding one death was 26. Similarly for patients who were independent in primary ADL functions before the stroke, there was a
difference in case fatality: 25.4% for patients treated in SUs and 29.1% for patients treated in GWs (OR 1.18 and CI 1.06-1.30; Figure 8). Among patients who were dependent upon ADL functions before the stroke, there was no difference in case fatality between patients treated in SUs and GWs (Figure 9).

**Figure 8.** Age-adjusted survival time in days for patients independent in primary ADL functions before stroke. Comparisons between patients treated in stroke units and general wards (Cox proportional hazard method).

Patients independent of help for primary ADL before the stroke. More people treated in SUs were still living in their own homes two years after the stroke, and they were still more often independent in primary ADL functions. After adjustment for differences in case mix, treatment in a SU was still an independent predictor for being independent of help for ADL two years after a stroke (Table 13).

**Figure 9.** Age-adjusted survival time in days for patients dependent in primary ADL functions before the stroke. Comparison between patients treated in stroke units and general wards (Cox proportional hazard method).
Table 13. Multiple logistic regression analyses of case fatality and ADL function at two-year follow-up. Only patients who were independent in primary ADL functions before the stroke were included. (Paper II).

<table>
<thead>
<tr>
<th>Case fatality at two-year follow-up</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 5,346</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impaired consciousness at arrival at hospital</td>
<td>3.16</td>
<td>2.84-3.53</td>
</tr>
<tr>
<td>Men</td>
<td>1.40</td>
<td>1.26-1.56</td>
</tr>
<tr>
<td>Living alone</td>
<td>1.13</td>
<td>1.01-1.27</td>
</tr>
<tr>
<td>High age</td>
<td>1.07</td>
<td>1.07-1.08</td>
</tr>
<tr>
<td>No examination with computed tomography</td>
<td>1.56</td>
<td>1.30-1.87</td>
</tr>
<tr>
<td>Cerebral haemorrhage</td>
<td>1.00</td>
<td>1.00-1.003</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>1.09</td>
<td>0.98-1.23</td>
</tr>
</tbody>
</table>

Interaction between type of living before stroke and SU/GW care
- Living at home before stroke and SU care Reference category
- Living at home before stroke and GW care |
- Living in an institution before stroke and SU care |
- Living in an institution before stroke and GW care |

Dependent on help for ADL at two-year follow-up
N = 3,206
<table>
<thead>
<tr>
<th>Dependent on help for ADL at two-year follow-up</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 3,206</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impaired consciousness at arrival at hospital</td>
<td>2.24</td>
<td>1.71-2.96</td>
</tr>
<tr>
<td>Stroke unit</td>
<td>0.79</td>
<td>0.66-0.94</td>
</tr>
<tr>
<td>Men</td>
<td>0.66</td>
<td>0.56-0.78</td>
</tr>
<tr>
<td>Living alone</td>
<td>1.04</td>
<td>0.87-1.24</td>
</tr>
<tr>
<td>High age</td>
<td>1.06</td>
<td>1.05-1.07</td>
</tr>
<tr>
<td>Examination with computed tomography</td>
<td>0.94</td>
<td>0.57-1.56</td>
</tr>
<tr>
<td>Cerebral haemorrhage</td>
<td>1.00</td>
<td>0.998-1.004</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>1.60</td>
<td>1.32-1.94</td>
</tr>
<tr>
<td>Institutional living before stroke</td>
<td>2.73</td>
<td>1.98-3.76</td>
</tr>
</tbody>
</table>
4.2.3 Use of oral anticoagulants in stroke patients with atrial fibrillation

In this study, 18,276 stroke patients in 75 hospitals were included. The number of AF patients was 4,538 (24.8%). The prevalence of AF was 21.3% for patients with first-ever stroke and 28.8% for patients with recurrent stroke.

At stroke onset

*First-ever stroke*. In the national Swedish sample, the proportion of AF patients that was treated with OA when the first-ever stroke occurred was 11.0% (323 out of 2932). The mean age of patients treated with OA, as primary prevention was 76.4 years as compared with 79.9 years among patients who did not receive treatment (p<0.001). Men and patients with diabetes were more often treated with OA, even after age adjustment.

The proportion on OA therapy when the stroke occurred ranged from 2.5% to 24.4% between hospitals. The corresponding proportion of AF patients who were treated with an antiplatelet agent was 43.8% in the national sample in RS and varied from 20.0% to 70.5% between the hospitals. OA or antiplatelet agents were used in 53.2% of all AF patients when their stroke occurred, with an inter-hospital range from 38.5% to 58.8%. There was no correlation between the proportion treated with OA and the proportion treated with antiplatelet agents in individual hospitals (r=0.13, p=0.51).

<table>
<thead>
<tr>
<th>Treatment with oral anticoagulants at onset</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;84 Reference category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75-84</td>
<td>3.06</td>
<td>2.09-4.45</td>
</tr>
<tr>
<td>65-74</td>
<td>3.13</td>
<td>2.04-4.81</td>
</tr>
<tr>
<td>&lt;64</td>
<td>4.24</td>
<td>2.46-7.31</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.32</td>
<td>1.04-1.72</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.53</td>
<td>1.16-2.00</td>
</tr>
</tbody>
</table>

Table 14. Prediction of treatment with oral anticoagulants on admission to hospital among AF patients with first-ever stroke (N=2,932).

The inter-regional variation in the proportion of patients treated with OA as primary prevention ranged from 8.4% to 13.5%. As shown in Table 14, younger age, male sex and presence of diabetes were found to predict use of OA as primary prevention independently of other potential predictors.

*Intracerebral haemorrhages in AF patients.* An intracerebral bleeding was more than twice as common among AF patients who were on treatment with OA on admission as compared with other AF patients.
(13.6% vs. 5.7%; OR 2.6, 95% CI 2.0-3.4). This excess risk was present even after adjustment for AF patients treated with OA being younger than other AF patients (OR 2.4, 95%CI 1.8-3.1).

**At discharge from hospital**

Among the 3,477 survivors of ischaemic stroke who had AF, 1,165 (33.5%) were discharged on OA in the national sample. The overall proportion of AF patients discharged on antiplatelet agents was 65.0% and the proportion discharged on any antithrombotic therapy was 90.9%. Patients discharged on OA were significantly younger than other patients (75.8 years vs. 81.3 years; p>0.001).

![Figure 10. Proportion of patients treated with oral anticoagulants and antiplatelet agents as secondary prevention in hospitals with more than 40 patients with atrial fibrillation (only patients with cerebral infarction who were discharged alive from hospital are included in this figure).](image)

The variation in use of OA in the secondary prevention after stroke in AF patients ranged from 16.4% to 61.9% between hospitals. The proportion of patients on antiplatelet agents at discharge ranged from 39.3% to 84.9%. Among those taking OA or antiplatelet agents the variation ranged from 76.7% to 100.0%. Figure 10 shows the total proportion of patients on any antithrombotic therapy in each individual hospital. The overlap between OA and antiplatelet agents was larger than expected. This is due to the design of the RS questionnaire. It is not possible to separate treatment with antithrombotic agents during hospital admission from treatment at discharge. However, most patients received either OA or antiplatelet agents resulting in a stroke negative correlation between use of OA and antiplatelet agents (r_s=-0.59, p<0.001). The inter-regional variation ranges from 29.9% to 40.6%.
As shown in Table 15, younger age, male sex, independence in primary ADL, intact level of consciousness on admission, being discharged home, and treatment in specific health care region independently predicted treatment with OA at discharge. There were no differences in the proportion discharged on OA between AF patients treated in stroke units and in general wards.

Table 15. Prediction of treatment with oral anticoagulants at discharge among patients with atrial fibrillation who were treated for cerebral infarction (N=2,592).

<table>
<thead>
<tr>
<th>Treatment with oral anticoagulants at discharge</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75-84</td>
<td>3.79</td>
<td>2.91 - 4.93</td>
</tr>
<tr>
<td>65-74</td>
<td>5.47</td>
<td>4.03 - 7.45</td>
</tr>
<tr>
<td>&lt;65</td>
<td>8.65</td>
<td>5.52 - 13.55</td>
</tr>
<tr>
<td>Independent primary ADL function</td>
<td>2.03</td>
<td>1.48 - 2.78</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.19</td>
<td>1.00 - 1.44</td>
</tr>
<tr>
<td>Fully conscious on admission</td>
<td>1.43</td>
<td>1.07 - 1.92</td>
</tr>
<tr>
<td>Discharged home</td>
<td>2.88</td>
<td>2.30 - 3.62</td>
</tr>
<tr>
<td>Health care region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>region 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>region 2</td>
<td>0.79</td>
<td>0.56 - 1.10</td>
</tr>
<tr>
<td>region 4</td>
<td>0.70</td>
<td>0.48 - 1.02</td>
</tr>
<tr>
<td>region 3</td>
<td>0.81</td>
<td>0.57 - 1.16</td>
</tr>
<tr>
<td>region 5</td>
<td>0.61</td>
<td>0.44 - 0.86</td>
</tr>
<tr>
<td>region 6</td>
<td>0.57</td>
<td>0.40 - 0.81</td>
</tr>
</tbody>
</table>

To explore if differences in the use of OA in AF patients reflected the practices of individual physicians/clinics treating stroke patients or a more general attitude in the hospital catchment area towards stroke prevention by OA, the use of anticoagulants before stroke and at discharge was compared. There was a moderate correlation between use of oral anticoagulation as primary and secondary prevention at hospitals that had registered more than 40 AF patients who were candidates for primary and secondary prevention that almost reached statistical significance ($r_s=0.35$, $p=0.06$).
4.3 Post-stroke fatigue

Of the 3,667 patients who did not always feel depressed at the two-year follow-up, 366 (10.0%) always felt tired. Another 1,073 often felt tired (29.2%) (Figure 11).

Figure 11. Prevalence of fatigue at two-year follow-up, in women, in men, and in all patients.

Variables at stroke onset predicting fatigue at 2 years

The mean age of the 3,667 patients included in the analysis, at the time of the stroke, was 71.8 years. Patients who always felt tired two years after the stroke were older at stroke onset than the rest of the patients (mean age, 74.5 years vs. 71.5 years, p-value<0.001). For many of the background variables there was a statistically significant association between more severe feelings of tiredness and less advantageous initial condition. Thus, fatigue two years after the stroke was more common among patients living alone before the stroke, living in an institution, being dependent on others for primary ADL functions before the stroke and having a recurrent stroke.

Results of the two-year follow up

Two years after the stroke, feelings of always being tired were more common among those patients who, after the stroke, were dependent upon help for both primary and secondary ADL and those patients living in an institutional living. Even after adjustments for other background variables were performed, there was a statistically significant increase in both primary and secondary ADL dependency with more severe feelings of fatigue. When analyses were restricted to
patients that lived at home before the stroke, a smaller proportion of the patients that were always tired had returned back to their own home.

**Case fatality one year after two-year follow-up (three years after the stroke event)**

Between the time of follow-up at two years and one year later (three years after the stroke event), 297 of the 3,667 patients had died. During this period, more patients that were always tired had died (17.3% vs. 7.1%, p<0.001). This was true even after adjustment for the background variables available at the 2-year follow-up.

**Table 16. Multiple logistic regression analyses of case fatality one year after two-year follow-up (three years after stroke event; N=3,637).**

<table>
<thead>
<tr>
<th>Case fatality one year after two-year follow-up</th>
<th>p-value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>High age</td>
<td>&lt;0.001</td>
<td>1.06</td>
<td>1.04-1.07</td>
</tr>
<tr>
<td>Men</td>
<td>0.002</td>
<td>1.46</td>
<td>1.14-1.86</td>
</tr>
<tr>
<td>Cerebral haemorrhage</td>
<td>0.04</td>
<td>1.64</td>
<td>1.02-5.30</td>
</tr>
<tr>
<td>Dependent primary ADL functions at follow-up</td>
<td>&lt;0.001</td>
<td>2.65</td>
<td>1.96-3.59</td>
</tr>
<tr>
<td>Impairment of speech</td>
<td>0.007</td>
<td>1.40</td>
<td>1.10-1.80</td>
</tr>
<tr>
<td>Co-habitant status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- living together</td>
<td></td>
<td></td>
<td>Reference category</td>
</tr>
<tr>
<td>- Living alone</td>
<td>0.42</td>
<td>1.13</td>
<td>0.84-1.53</td>
</tr>
<tr>
<td>- missing patients</td>
<td>&lt;0.001</td>
<td>2.25</td>
<td>1.64-3.06</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Never or sometimes</td>
<td></td>
<td></td>
<td>Reference category</td>
</tr>
<tr>
<td>- Often</td>
<td>0.045</td>
<td>1.31</td>
<td>1.01-1.71</td>
</tr>
<tr>
<td>- Always</td>
<td>&lt;0.001</td>
<td>1.85</td>
<td>1.35-2.54</td>
</tr>
</tbody>
</table>
5 DISCUSSION

5.1 Validity of the Riks-Stroke register

5.1.1 Case validity

Coverage

Riks-Stroke is the first register assessing the quality of stroke care in a whole country. Earlier studies have shown that 90% - 97% of patients with stroke are treated as inpatients. After consideration of selection bias, it seems reasonable that hospital-based stroke registers can be used in studies of acute stroke care in Sweden.

Riks-Stroke permits comparisons of processes and outcome of stroke care between all hospitals and regions in Sweden. The participation in the RS register is voluntary, but since 1998 all Swedish hospitals admitting stroke patients have joined. In some hospitals, the register is still in a build-up phase and is incomplete. Our validation study (Section 3.3.1) showed that approximately three quarters of all acute stroke events receiving in-hospital care in Sweden are included each year. A seemingly low coverage of stroke events in RS according to NDR is partly caused by different criteria for stroke diagnoses in RS and NDR. This was shown by the fact that many patients who had had a previous stroke but who were not diagnosed as a new stroke event during the present hospital admission received a new acute stroke diagnosis. According to the manual for ICD-10 diagnoses, the acute stroke diagnosis should remain for 12 months after stroke. In the RS manual, a patient should be included in the register if he/she is treated for an acute stroke, and diagnosed as an acute stroke, during the current hospital admission. When assessing the coverage of RS by comparison with those with definite strokes according to validation criteria in NDR, there was a higher level of agreement. Also previous studies have shown that NDR includes too many stroke diagnoses.

Administrative databases, as those based on hospital discharge records, have been shown to over diagnose stroke. Between 60% and 94% of stroke events have, in validation studies, been shown to be a
definite stroke 219-223. As discussed in the Methods section 3.2.1, the epidemiological coverage of RS is probably underestimated. The estimate of 27,000 stroke events probably correlates better to the number of first-ever stroke and not all strokes (first-ever plus recurrent). In this study we have also shown that the coverage of RS according to definite stroke in NDR agreed well with coverage assessed by epidemiological estimates of occurrence of new stroke events in Sweden. Also at the hospital level, the two methods for calculating coverage rate show consistency. With thoroughly performed analyses of missing patients we have shown that we have a stroke population in RS that is reasonably representative of the stroke population in Sweden.

**Case ascertainment**

Stroke events in NDR that are included in RS as well, are more often registered with stroke as the main diagnosis in NDR, indicating a more certain stroke diagnosis among those also included in RS.

Those patients with stroke events that are not included in RS are more often treated in GWs and less often in organised stroke care. Also previous studies have shown that hospitals with an organised SU care include more patients in RS 15. This reflects the organisational structure of RS at local hospitals. The SUs have the most interest in stroke care and co-ordinates the inclusion of stroke patients from their own ward as well as from other wards in the hospital. This was shown already in 1998 when a telephone interview was performed with the administrative person for RS at each hospital 224. Mentioned as main reasons for not including stroke events in RS were lack of time and too few hospital beds in the SU. The present study also showed that patients treated in hospitals for other conditions than stroke at stroke onset are probably not moved to the SU and subsequently not included in RS.

The telephone interview also showed that patients who die early after admission and those who have only mild strokes are less often included in RS. In this study, this was confirmed by the tendency towards patients who died within the first month and in particular those who died during the first week, were not included in RS. Case fatality rates are most certainly underestimated in RS.

Patients with definite strokes included in NDR but missing in RS during 1999 were younger than patients with definite strokes included in NDR as well as in RS. During the same year a comparison between all stroke events in NDR and stroke events in RS showed the opposite result. However, this is probably due to the fact that the heterogeneous group of patients with uncertain strokes and those who had probably not had a stroke prior to the actual hospital admission, are included in the comparison between all stroke events in NDR and stroke events in RS. This patient group consists mainly of elderly patients.
However, differences between the two registers in age and living situation have decreased between 1999 and 2001. Also number of hospital admissions with stroke diagnoses decreased in the NDR between 1998 and 2001. This suggests that the decrease in differences between stroke events in NDR that are included in RS and stroke events that are missing in RS is due to (a) improvement of stroke diagnoses in NDR and (b) to stroke events in RS becoming increasingly representative for stroke events in Sweden.

To ensure that the patient population was reasonably representative, we excluded hospitals in which the registration was obviously incomplete in two of the sub-studies (Paper I and III). Patients treated in excluded hospitals were shown to be older, more dependent in ADL before stroke, received care in SUs less often, and had a lower case fatality. In hospitals excluded from analyses, the use of OA in AF patients at discharge was lower than in included hospitals. These results agree well with the findings from the study of case validity of RS, and it is reasonable to assume that the patients reported on in those sub-studies were more representative for a national sample of stroke patients than those who had been excluded.

The other main reason for exclusion in sub-studies was a missing three-month follow-up or a missing two-year follow-up. Those patients for whom a follow-up was not performed had a worse pre-stroke condition. The results in this study should therefore be interpreted carefully for this group of patients.

Routine collection of data for evaluation of quality is an essential component of stroke care. Our validation study showed that SUs were more successful at including patients in RS. The ability to manage quality assessment systems is another argument for the superiority of SUs to manage stroke patients.

5.1.2 Item validity

Accuracy of data

In the data collection process, the strategy of RS has been to give coverage a higher priority than details. Thus, data collection is kept very simple. This is to facilitate for hospitals with limited interest (or resources) for stroke care to participate; such hospitals may be those with the greatest potential to benefit from a quality assessment register. In scientific studies, this strategy has the advantage that it produces very large patient numbers and narrows confidence intervals around the estimates. The drawback is that only few clinical variables are available for studies of possible determinants of interventions and outcomes of interest.
Also the two-year follow-up study was designed to include a very large number of patients, many of whom were very old and had severe impairments after stroke. Therefore, a mail questionnaire with simple questions and response alternatives was used. The data should therefore show a high sensitivity, at the expense of the specificity. Since most information in the three-month follow-up questionnaire and the two-year follow-up questionnaire was to be assessed on the actual day of responding to the questionnaires, recall bias is unlikely.

Data in RS showed a reasonably good concordance with information in hospital records for most of the variables. Variables that showed a lower agreement had a high frequency of missing data in hospital records or the data were difficult to interpret. To be able to evaluate national feedback data in routine practice, information on patient and hospital admission has to be included uniformly. There are uniform guidelines on how to register information about patients in RS, and hospitals that include patients in RS are therefore instructed to follow the RS guidelines. For optimal implementation of the guidelines, constant support and feedback are needed.

Validation of RS forms

The questions assessing primary ADL in RS show good agreement with the Barthel index. The Barthel index has shown to have good validity and reliability and has been shown to be the most reliable disability scale. It is therefore reasonable to assume that that index can be used as a measure of primary ADL. However, objections towards Barthel index have regarded a ceiling effect and limitations in self-reporting among patients above 75 years of age. The question assessing fatigue showed good correlation with BFI. However, the fatigue question did not discriminate between never feeling tired and sometimes feeling tired nor between often tired and always tired. Therefore, the classification of fatigue into four categories should be performed with caution.
5.2 Management of stroke

5.2.1 Sex differences

Our study showed that women were more dependent than men upon help and support from next-of-kin. They also had a greater need of help from health care and community that had not been sufficiently met. This is an essential issue for outcome after stroke among women as they are more often living alone. As discussed in section 1.5.5, good social support is associated with faster and more extensive recovery of functional status after stroke, and large social networks lower the risk for institutionalisation.

At discharge from hospital, women received antithrombotic stroke prevention less often than men. This is mainly because of differences in the proportion treated with OA. As discussed in section 1.5.4 this is in agreement with previous observations that women with AF are less often treated with OA. This may seem paradoxical since women with AF have as high risk for embolism and long-term mortality as men, and the beneficial effect of OA has been shown to be even greater among women. The differences between men and women remained after adjustment for age in the present study. It could well be that the differences in how men and women with stroke are treated are not the result of rational medical considerations.

Level of consciousness is an indicator of stroke severity, and decreased consciousness is one of the strongest predictive factors for poor outcome after stroke. In our study, an impairment of consciousness was slightly more common among women. In contrast to this finding, there were no differences in case fatality between men and women. Among stroke survivors, more women were institutionalised at the three-month follow-up. Differences in pre-stroke condition, in co-morbidities, in medical management, and in the need and distribution of help and support explain sex differences in functional outcome after stroke. Nevertheless, these results were valid even after adjustment for other predictive variables and after analyses of the subgroup of patients being independent in ADL and living at home with a close relative before stroke onset (data not shown).

Strategies to reduce the apparent sex difference in the management of stroke need to be developed. As a first item on such an agenda, the mere fact that sex differences exist should be more widely recognised among those who care for stroke patients.
5.2.2 Long-term effects of stroke unit care

Several controlled randomised studies as well as a meta-analysis have proven a beneficial effect of SU care. Why do we need observational studies as well? An intervention that has proven effective in experimental settings has to be evaluated also in routine clinical practice. Does the effect remains and if so, to what extent? As discussed in section 1.3, a diminished effect may have several reasons. Patients and SUs in routine health care are more heterogeneous than in controlled studies. Less strict definitions of interventions also contributes.

In the subgroup of patients who were independent of help before the stroke, the differences in case fatality and ADL dependence were present three months after the stroke. The short-term beneficial effects in routine clinical practice in this patient group in Sweden were shown already in 1996. Patients who were living independently and who were fully conscious on admission had lower case fatality rates and could more often return home. No significant differences were shown for patients who had an impaired consciousness on admission. These results agree with long-term findings from the present study (Paper II).

In the total stroke population, as well as in the group of patients that were independent in primary ADL before the stroke, patients treated in SUs had an improved outcome more than two years after stroke compared to patients treated in GWs. Patients who were ADL dependent before stroke did not show any beneficial effect of SU care. In conclusion, no beneficial effects of SU care were shown for patients who were functionally impaired, irrespective of if the impairment was present before stroke or if the patient was severely affected at stroke onset.

The sub-group of patients that was dependent upon help for ADL before the stroke was much smaller, and the results for them are more inconclusive. The literature shows diverse results for this group of patients. As discussed in section 1.6.3, the studies from the SUTC and other studies have concluded that SU care has a beneficial effect in all subgroups of patients, and that SUs should treat an unselected population of stroke patients. In some studies patients who were functionally impaired before stroke were excluded from analyses. Results from a previous study that included a more heterogeneous study population suggested that the beneficial effects of treatment in SUs might be less pronounced for elderly and more severely disabled patients.

Several explanations are plausible for not finding any beneficial effect of treatment in an SU for patients who were functionally impaired before the stroke in our study. Because of an already existing functional impairment among these patents, the rehabilitation potential was probably smaller than in other patients. Their impairments could be so severe that interventions taken place in an SU could not affect the
outcome. It is also possible that our study design did not allow us to discover possible beneficial effects. More detailed measurements of improvements may be needed for this group of patients. Data collection in RS is kept very simple and only few background variables are registered. Adjustments for differences in co-morbidities before the stroke and other factors that influence outcome after the stroke would need to be included for these patients that suffer from diseases and functional impairments already before the stroke.

The need for, and satisfaction with received rehabilitation, was similar for all patients, irrespective of type of acute treatment. The differences in outcome at follow-up can therefore not only be ascribed to differences in care and support late after stroke but also to differences in background variables at time for the stroke and type of treatment during the acute phase. To minimise the possible influence of differences in background variables, we performed multivariate regression models, including background variables available in the RS register. These results confirm several other controlled randomised studies on long-term outcome after treatment in SUs.

Earlier studies that focus on differences in quality of life between patients treated in SUs and in GWs were published by Indredavik et al. and Juby et al. Indredavik showed statistically significant differences in all aspects of the Nottingham Health Profile except for pain. In the study performed by Judy, patients treated in SUs showed better psychological outcome. In contrast, our study did not show any differences in estimated health or cognitive abilities two years after the stroke. The heterogeneous study population and organisation of the SUs at the different hospitals might have diluted any possible beneficial effects observed in randomised trials.

In conclusion, in this nation-wide observational study, long-term beneficial effects of treatment in SUs applied in routine settings were shown for patients who had been independent of help for ADL. No benefits were shown for patients who had been dependent upon help for primary ADL before the stroke. Further studies on this group of patients with more detailed outcome are needed.

5.2.3 Use of oral anticoagulants in stroke patients with atrial fibrillation

This study confirmed the underuse of OA among stroke patients with AF. In addition, significant regional differences were shown even within a highly developed country as Sweden.

The prevalence of AF patients treated with OA as primary prevention in Sweden was not known in this study. Instead, the use of OA at stroke onset in AF patients is assumed to reflect primary prevention among AF patients. Those patients reported on here were
anticoagulants failures, i.e., those patients who were treated with OA and who still suffered a stroke event. The proportion of OA-treated patients among AF patients admitted for stroke is supposed to reflect the proportion of AF patients treated with OA. This is based on the postulate that the relative effects of anticoagulation to prevent stroke are the same in different hospital catchment areas. In addition, Sweden is a demographically homogenous country and there are uniform Swedish national guidelines for anticoagulant treatment to prevent stroke in AF patients. Non-cardioembolic AF associated strokes are likely to occur among OA treated AF patients with stroke. Nevertheless, it is assumed that they are equally distributed throughout the country and any variations should not substantially have influenced the results in this study. It is therefore unlikely that variations, other than proportion of AF patients treated with OA, can explain but a small fraction of the variations in the use of anticoagulants at stroke onset in Sweden.

In this national sample, 11% of the AF patients with a first-ever stroke were treated with OA on admission and approximately half of the AF patients received any antithrombotic therapy. Similar results, where only 8.4% of AF patients hospitalised for first-ever stroke were anticoagulant-treated, were found in a European study of 22 hospitals. In a Canadian study of 3,575 patients hospitalised with AF, 16% received treatment with OA on admission. The prevalence for OA as secondary prevention was also low in several studies. In the previously mentioned Canadian study, 32% received treatment with OA at discharge from hospital. Only 12% of the AF patients admitted to hospital for a recurrent stroke were on treatment with OA in Denmark. In our study, 21% of patients with a recurrent stroke were on treatment with OA and 33.5% of all stroke patients with AF were on OA at discharge. Direct comparisons between the national sample in our study and the results in the previously published studies are hampered by varying inclusion criteria and patients with high bleeding risk and other contraindications often being excluded. The prevalence of treatment with OA varies between 15% and 79% in AF patients without contraindications, and most of these studies conclude that there is an underuse of OA for prevention of stroke in AF patients.

Younger age is one of the strongest determinants for the chance of receiving treatment with OA, both for primary and secondary prevention. The mean age of stroke patients in Sweden is 75 years and 80% of the AF patients are 75 years or older. In our study, patients with an age 75 years or older had a chance to be treated with OA as primary that was half, and a chance to receive secondary prevention that was only a third as compared with patients younger than 75 years. Prevention of stroke in older patients is a challenge and has been discussed more extensively in section 1.7.3.
As shown in our study with limited background data and other studies, differences in case mix did not determine all variation in the use of OA. Also after excluding those patients who were discharged to institutional living and who probably were most severely disabled, barely half of the AF patients received OA. There were still significant differences between regions.

There was a modest correlation between hospitals in the use of OA on admission to hospital and at discharge, whereas there were no differences in proportion treated with OA between SUs and GWs. This indicates that general attitudes and traditions may be one of the determinants of the use of anticoagulants to prevent stroke in AF patients.

In the Swedish national guidelines for stroke care, published in 2000, OA is recommended as a first choice in the primary and secondary prevention of stroke in AF patients. Despite this, local factors seem to determine if patients with AF get access to optimal prevention of stroke or not. It is urgent to secure a good and equal care for AF patients, at risk for a new or recurrent stroke, independently of where they receive treatment. Physicians need education to make better judgements on risks and benefits, and they need a health care organisation that optimises condition for treatment with OA and make it a favourable alternative. Quality control systems are necessary tools for balancing risks and benefits. Since 1985 a Swedish national monitoring system for hospital-based and centralised OA clinics has gradually developed to supply feedback on OA treatment. When doctors and patients become more secure in optimising the effect of OA treatment and minimising the risks, the inclination to use OA will probably increase.

5.3 Post-stroke fatigue

In the present study the prevalence of patients who were always tired was approximately 10%, and another 29% were often tired (Paper IV). The majority of patients with moderate to severe and disabling post-stroke fatigue have probably been identified, as the sensitivity according to BFI was 100%. However, this was done at the expense of specificity that was shown to be 75%, meaning that the prevalence of severe fatigue could have been overestimation. On the other hand, patients who were alive at the time of the two-year follow-up but did not respond to the follow-up questionnaire or those who always felt depressed, and therefore not included in analyses, were on average older and more disabled before the stroke. This indicates that more
patients with fatigue probably could be found among those who did not return the follow-up questionnaires. This would lead to an underestimate of the prevalence of post-stroke fatigue. Overall, the prevalence rates presented here seem to reflect reasonably well the situation among survivors two years after stroke that are not severely depressed.

An important issue to consider when using multidimensional scales is that many stroke patients suffer from cognitive impairments, which make it difficult to complete complex questionnaires. An optimal questionnaire for post-stroke fatigue should be short and aimed directly towards characteristics of fatigue associated with stroke. As this study was designed to include a very large number of patients, many of whom were very old and had severe impairments after stroke, a mail questionnaire with a single item strategy was used. Both questions and possible answers had to be easily understandable because the patients had to be able to fill in the questionnaire without help.

Prevalence of fatigue in other studies closely coincide with our prevalence estimate of 39% being always or often tired two years after stroke. However, differences in case-mix and the use of different self-estimation scales to study post-stroke fatigue hamper direct comparisons of the prevalence of post-stroke fatigue between studies. To define various forms and severity of post-stroke fatigue and to help to understand underlying mechanisms, a stroke-specific instrument to measure fatigue is probably needed.

A group at particularly high risk for post-stroke fatigue can be identified. Patients with post-stroke fatigue were older and had a less advantageous condition before the stroke. There was also a small female preponderance for post-stroke fatigue. The study design did not allow us to differ between fatigue present already before the stroke and fatigue evolving after the stroke. Tiredness has previously been shown to be a determinant of disability among non-disabled old people. In our study, fatigue was associated with a more negative outcome two years after stroke even after adjustment for differences in baseline variables. This indicates that fatigue also is a consequence of stroke and that this affects the outcome.

At follow-up, institutional care, being ADL dependent, having speech impairment and a feeling of poor general health were all factors associated with fatigue. The association between fatigue and an adverse outcome is probably reciprocal. Impairment in functional ability and general health probably induces a condition with fatigue, and severe fatigue affects functional ability and general health. It seems that post-stroke fatigue results from a combination of an organic brain lesion and an inappropriate coping with a new life situation after the stroke. Fatigue is associated with other mental and physical consequences of stroke, perhaps most importantly depression. However, as shown in this and previous studies, after excluding patients with depression, there is...
still a group of patients with symptoms of fatigue. In sensitivity analyses that also excluded patients who always or often felt depressed, fatigue still merged as an independent predictor of poor functional outcome. Furthermore, in multivariate logistic models with depression as one of the explanatory variables, fatigue was still an independent predictor for being dependent in primary ADL functions and for perceiving the general health as very poor.

The close association between depression and poor survival after stroke has been amply demonstrated. We now show, for the first time, that fatigue is also an important predictor of death late after stroke, even after adjustment for depression and other important predictors of survival. It has previously been shown that vital exhaustion, a syndrome of unusual fatigue and loss of energy, increases irritability, depressive symptoms, and increases the risk of myocardial infarction and other manifestations of coronary heart disease.

As discussed in section 1.7.4, fatigue in association with other diseases and conditions are treated in many different ways. However, in different diseases or medical conditions, there are probably different mechanisms that cause the fatigue and specific treatments would be needed. Clinical trials to find an effective treatment for patients with post-stroke fatigue are warranted.

5.4 The national impact of Riks-Stroke

The interest for and development of stroke care has increased dramatically during the last decades. RS has contributed to this development by monitoring stroke care and by supplying feedback data on process and outcome of stroke care. In addition, RS has catalysed this positive development by continuous communication with the personnel working with stroke patients in hospitals. Results from RS have been available for national inquiries on stroke care and for the development of the Swedish National Guidelines for Stroke Care.

After this systematic evaluation of how representative RS is for the stroke population in Sweden, the next challenge is to systematically evaluate to what extent a national monitoring system such as RS contributes to improvements in clinical praxis.
6 CONCLUSIONS

The validation studies of Riks-Stroke were performed to ensure that information in Riks-Stroke is representative for stroke events in Sweden.

- Three quarters of all stroke events in Sweden are included in Riks-Stroke. The coverage of stroke patients and the selection of patients included vary between hospitals, counties and regions. Results have to be interpreted in consideration to missing patients and case mix.
- Stroke units are superior in the ability to manage quality assessment systems.
- Stroke patients who are not included in the national sample of Riks-Stroke more often have an uncertain stroke diagnosis. There are tendencies towards these patients being younger and less dependent in ADL functions before stroke. Our validation studies suggest that case fatality rates are somewhat underestimated in Riks-Stroke.
- Data in Riks-Stroke show good concordance with data documented in hospital records.

As Riks-Stroke provides a continuous monitoring of stroke care, differences in management and outcome between patient groups can be discovered. To develop strategies that optimise the outcome for all stroke patients, these differences need to be studied in more detail.

- When compared with men, women with stroke are more often living in institutions three months after stroke. This is partly explained by a worse pre-stroke condition, differences in co-morbidities and need for and distribution of help and support.
- Female stroke patients less often receive secondary stroke prevention. In particular, women with atrial fibrillation receive less often oral anticoagulants at discharge from hospital.
Riks-Stroke evaluates results from controlled randomised studies in routine clinical practice. A large number of controlled randomised studies on stroke unit care have been performed, and results from Riks-Stroke have previously shown that the short-term beneficial effects are valid also in routine clinical practice.

- There are long-term beneficial effects of SU care in clinical practice for patients who were independent in ADL functions before the stroke.
- For those patients who are ADL dependent before stroke the results are more inconclusive.

As Riks-Stroke includes all hospitals admitting stroke patients during the acute phase, national variations in stroke management can be studied. In the National Guidelines for Stroke Care, treatment with oral anticoagulants is recommended as first-choice in the primary and secondary prevention of stroke in patients with atrial fibrillation.

- There are wide variations in the use of oral anticoagulants in stroke patients with atrial fibrillation, not only between hospitals, but also between counties and health care regions.
- Local factors, general attitudes and traditions seem to be major predictors of the use of oral anticoagulants in stroke patients with atrial fibrillation.

Riks-Stroke provides data on stroke patients throughout Sweden. The register is a valuable resource for follow-up studies of long-term consequences.

- Post-stroke fatigue is an unexplored long-term term consequence after stroke that is frequent, even late after stroke.
- Post-stroke fatigue was an independent predictor for functional dependence, institutional living and death late after stroke.
IMPLICATIONS FOR THE FUTURE

- All data used for monitoring the quality of stroke care should be included in routine medical records. Preferably, data extraction for quality register should be automatic from computerised medical records. This will ensure next-to-complete coverage. An even larger challenge for the future is how to monitor care late after stroke, supplied by primary care and municipal care.

- Strategies to reduce apparent sex differences in stroke management and outcome have to be developed. As a first item on such an agenda, the mere fact that sex differences exist should be more widely recognised.

- Further studies should be performed on the beneficial effects of stroke unit care in routine clinical practice for stroke patients who are functionally dependent before stroke.

- To secure a good and equal care independently of where the patient receives treatment, it is urgent to eliminate differences between hospitals, counties and regions in the prevention of a first-ever or a recurrent stroke in patients with atrial fibrillation.

- So far, there are no effective treatments for the severe long-term consequence, post-stroke fatigue. Nor have any controlled studies been performed on treatment for post-stroke fatigue. Intervention studies are needed.
ACKNOWLEDGEMENTS

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His enthusiasm and knowledge has made Riks-Stroke into one of the most prominent Swedish national quality registers and the only national stroke register in the world.

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For giving me prerequisites to develop

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For sharing my life and making it meaningful
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RIKS-STROKE - ACUTE PHASE

Personal ID number | ________ | ________ | ________ | ________ | ________ | ________
Sex 1= male 2= female | ____ |
Name (optional)
Address (optional)
Telephone (optional)
Optional information (for instance, name and telephone number of family member)

Reporting hospital | ________ | ________ | ________
Department/ward | ________ | ________ | ________ | ________ | ________
Date of registration | ________ | ________ | ________ | ________ | ________ Year/Month/Day (yy/mm/dd)
Competed by (name of person who completed this form) ............................................................... 

PRIOR TO STROKE

Living
1= in own home without community support
2= in own home with community support
3= living in a community facility (for instance service flat with full board, old peoples’ home, nursing home)
5= other (fill in) Other ............................................................................................................

Living alone
1= the patient lives on his/her own
2= the patient lives with a spouse/partner or another person, for instance family member

Mobility
1= the patient was able (prior to this illness) to move around without supervision indoors as well as outdoors (use of support or walking stick allowed)
2= the patient was able to move around by his/her own indoors but not outdoors
3= the patient was assisted by another person when moving around or he/she was bedridden

Toilet visits
1= the patient managed toilet visits on his/her own
2= the patient was unable to go to the toilet unaided, or used bedpan or incontinence pads or needed assistance in wiping him/herself or in dressing

Dressing
1= the patient was able to dress without assistance, including outdoor clothes, socks/stockings and shoes, or needed assistance only in tying shoelaces
2= the patient needed assistance to fetch clothes, or needed assistance in dressing/undressing or remained in his/her night-clothes

RISK FACTORS

Previous stroke? (NOTE that TIA is not included) 1= yes 2= no 9=not known

Atrial fibrillation at onset of stroke? (including intermittent fibrillation or flutter) 1= yes 2= no 9=not known

Diabetes, previously known or newly diagnosed? 1= yes 2= no 9=not known
Treatment for hypertension at onset of stroke?
1= yes  2= no  9= not known

Is the patient a smoker?
1= yes  2= no  9= not known

Level of consciousness on arrival to hospital
1= fully awake (RLS 1)
2= drowsy but responding to stimulus (RLS 2-3)
3= unconscious (RLS 4-8)
9= not known

CT scan during hospital stay
1= yes  2= no  9= not known

Antithrombotic therapy (acute phase = first 7 days from admission to hospital)

Response alternatives
Patients on treatment at onset
1= yes, and continuing
2= yes, but discontinued and not re-started
3= yes, but discontinued, planning to re-start

Patients in whom treatment is initiated during or after the acute phase
4= yes, initiated during the acute phase
5= yes, initiated or planned to be initiated after the acute phase

Other response alternatives
6= no
7= patient included in a drug trial
9= not known

Drugs
Aspirin; for instance [brand names]
Antiplatelet agents (except aspirin); for instance [brand names]
Oral anticoagulants, for instance [brand names]
Anticoagulants, injection or infusion (for instance [brand names]) for stroke
Anticoagulants, injection or infusion (for instance [brand names]) for prevention of venous thrombosis

Thrombolysis, for instance [brand names]

Time point for start of thrombolytic treatment (hour minute)

Intracranial bleeding with clinical symptoms <36 h after start of treatment (but be confirmed by CT scan or autopsy)
1= yes  2= no  9= not known

Did the patient improve markedly (for instance marked recovery of speech or paresis) within 2 h of onset of treatment
1= yes  2= no  9= not known
## SEQUENCE OF CARE

### A. ACUTE MANAGEMENT
(refers to the first episode of hospital care for the present stroke)

<table>
<thead>
<tr>
<th>Date of onset</th>
<th>(yy/mm/dd)</th>
<th>Time of onset of symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of admission</td>
<td>(yy/mm/dd)</td>
<td>Time of arrival</td>
</tr>
<tr>
<td>Date of discharge</td>
<td>(yy/mm/dd)</td>
<td></td>
</tr>
</tbody>
</table>

**First admitted to**

1. General ward
2. Stroke unit
3. Admission/observation ward
4. Intensive care unit
5. Other (fill in)

**First department**

1. Medicine
2. Neurology
3. Geriatrics
4. Other

**Continued care during the acute phase**

1. General ward
2. Stroke unit
3. Admission/observation ward
4. Intensive care unit
5. Other (fill in)

**Subsequent department**

1. Medicine
2. Neurology
3. Geriatrics
4. Other

### B. LATE MANAGEMENT
(refers to continued rehabilitation of acute stroke within the same health care system)

<table>
<thead>
<tr>
<th>Date of admission</th>
<th>(yy/mm/dd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of discharge</td>
<td>(yy/mm/dd)</td>
</tr>
</tbody>
</table>

---

### DISCHARGED TO

1. Own home
2. A community facility (for instance service flat with full board, old peoples' home, nursing home)
3. Other acute-care department
4. Geriatric/rehab department
5. Dead during hospital stay
6. Other
7. Not known

**Other (specify)**

---

### STROKE DIAGNOSIS

1. Intracerebral hemorrhage
2. Cerebral infarction
3. Unspecified acute stroke
4. TIA/cerebral ischemia/transient within 24 h (optional)

---

### DECEASED

**Date (date when the patient died) (yy/mm/dd)**

**Autopsy**

1. Yes
2. No
3. Not known
RIKS-STROKE - 3 MONTHS’ FOLLOW-UP

To be filled in by staff before the patient is discharged

<table>
<thead>
<tr>
<th>Personal ID number</th>
<th>___________ ___________ ___________ ___________</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name (optional)</td>
<td></td>
</tr>
<tr>
<td>Address (optional)</td>
<td></td>
</tr>
<tr>
<td>Telephone (optional)</td>
<td></td>
</tr>
<tr>
<td>Reporting hospital</td>
<td>___________</td>
</tr>
<tr>
<td>Department</td>
<td>___________</td>
</tr>
<tr>
<td>Date of follow-up (year, month, day)</td>
<td>___________ ___________ ___________</td>
</tr>
</tbody>
</table>

The questionnaire is to be filled in 3 months after onset of stroke

Are you satisfied with the care you received in hospital?

1  I __ I = Very satisfied
2  I __ I = Satisfied
3  I __ I = Dissatisfied
4  I __ I = Very dissatisfied
8  I __ I = Don’t know

*comment.................................................................................................................................................

Have you got any support from the health care or the community social services after the hospital stay?

1  I __ I = Yes
2  I __ I = No, but I would have liked to have support
3  I __ I = No, no need or wish for support
8  I __ I = Don’t know

*comment.................................................................................................................................................

If yes, what type of support have you got (several alternatives are possible)?

   I __ I = Day-care rehabilitation
   I __ I = Home rehabilitation
   I __ I = Short-term institutional care for rehabilitation
   I __ I = Other support (for instance physician, nurse, physiotherapist, occupational therapist, social worker, speech therapist)
   I __ I = Don’t know

If yes, have your needs of support been met?

1  I __ I = Yes
2  I __ I = No
8  I __ I = Don’t know

*comment.................................................................................................................................................
Are you, today, dependent on a family member/next-of-kin for help/support?

1. __I__ = Yes, partly dependent
2. __I__ = Yes, entirely dependent
3. __I__ = No, not at all
8. __I__ = Don't know

**Comment**

Is there any planning made by the staff of community social services, or the health care, for your future care and rehabilitation?

1. __I__ = Yes
2. __I__ = No
8. __I__ = Don't know

If yes, have you yourself participated in the planning?

1. __I__ = Yes
2. __I__ = No
8. __I__ = Don't know

**Comment**

Do you feel depressed?

1. __I__ = Nearly never
2. __I__ = Sometimes
3. __I__ = Often
4. __I__ = Always
8. __I__ = Don't know

If you feel depressed often or always – have you got any treatment by a doctor?

1. __I__ = Yes
2. __I__ = No
8. __I__ = Don't know

**Comment**

How do you regard your general health status?

1. __I__ = Very good
2. __I__ = Fairly good
3. __I__ = Fairly bad
4. __I__ = Very bad
8. __I__ = Don't know

**Comment**
Where are you staying now?

1 ___ I = in own home without community support
2 ___ I = in own home with community support
3 ___ I = living in a community facility (for instance service flat with full board, old peoples’ home, nursing home)
4 ___ I = in acute-care hospital (for example medical, neurological or surgical ward)
5 ___ I = other ................................................................................................................................................
6 ___ I = in a geriatric/rehabilitation unit

Do you live alone?

1 ___ I = Yes, I am living entirely on my own
2 ___ I = No, I share the household with spouse/partner or another person, for instance brother, sister, child, parents

How mobile are you now?

1 ___ I = I can move around without help both indoors and outdoors
2 ___ I = I can move without help indoors but not outdoors
3 ___ I = I need another person’s help to move

Do you receive help from anybody to go to the toilet?

1 ___ I = I can manage toilet visits without assistance
2 ___ I = I need help to go to the toilet

Do you receive help with dressing/undressing?

1 ___ I = I can manage to dress/undress without help
2 ___ I = I need help dressing/undressing

Who filled in this questionnaire?

1 ___ I = The patient him/herself in writing
2 ___ I = The patient with the help of a family member
3 ___ I = The patient by telephone
4 ___ I = Other person
5 ___ I = The patient at an out-patient visit to the hospital
6 ___ I = Medical staff

Thank you for your help and co-operation!
Please return this questionnaire to

(address)