Quality of life, Coping and need for Support during the ALS disease trajectory

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Abstract

The overall aim of this thesis was to investigate quality of life, coping and emotional distress (i.e. anxiety and depression) among newly diagnosed ALS patients. An additional aim was also to investigate relatives’ experiences of the care for the patient and the support they received for themselves during the disease progression.

The most nominated areas of importance for the patient’s overall QoL were family, friends and own physical health. Most patients rated their QoL as good, which did not change at subsequent measurement, despite their physical function having changed for the worse during disease progression. Some patients had symptoms of clinical anxiety and depression during the first year after diagnosis. The total quality of life score did not correlate with physical function but with depression early on after diagnosis. Most patients used support and independence as strategies to cope with the disease during the first six months after diagnosis. There were few changes early on after the diagnosis, and the patients used several different strategies. The results show that the use of coping strategies remained stable over time. Both physical function and emotional distress correlated significant with different coping strategies, with some variation during the disease progression. Relatives experienced the care of their loved one as positive and based on the patient’s needs and desires. The treatment, knowledge, support and help from the staff were important for the relatives’ feeling of security. Different factors influence the use of support for themselves. The relatives did not think of their own needs, but their focus was rather on the patient.

The results of the thesis highlight the importance of providing support both to patients and their relatives during the disease progression. With early and regular evaluation on quality of life, coping and emotional well-being among the patients, the health professionals may be able to support the patients based on their specific needs, which probably will increase their quality of life.

Keywords: amyotrophic lateral sclerosis, quality of life, coping strategies, emotional well-being, relatives, care, support

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Abbreviation

ALS  Amyotrophic Lateral Sclerosis
ALS FRS-R  The revised Amyotrophic Lateral Sclerosis Functional Rating Scale
BMI  Body Mass Index
FALS  Familiar Amyotrophic Lateral Sclerosis
FVC  Forced Vital Capacity
HADS  Hospital Anxiety and Depression Scale
   HADSa  Hospital Anxiety and Depression Scale – Anxiety
   HADSD  Hospital Anxiety and Depression Scale – Depression
HRQoL  Health Related Quality of Life
iQoL  individual Quality of Life
MNDCS  Motor Neuron Disease Coping Scale
QoL  Quality of Life
SALS  Sporadic Amyotrophic Lateral Sclerosis
SEIQoL-DW  Schedule of Evaluation of Individual Quality of Life – Direct Weighting
SMA  Spinal Muscle Atrophy
WHO  World Health Organisation
Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal disease, affecting both physical function and psychological well-being of the patient. Due to the disease progression, both the patient and relatives have to continually adjust to new losses in the patient’s physical function and new situations that arise in their daily living. To be able to help and support such patients, we need more knowledge about the disease, specifically regarding physical function, emotional well-being, coping strategies and quality of life from diagnosis and as it progresses. Taking into consideration the patient’s views is important for a more complete understanding of services needed and how to prioritise. The disease affects not only the patient, but also the whole family due to the different symptoms that occur during the disease duration. Experiences had by the relatives while caring for the patient and recognising the caretakers’ need for support are important aspects that can be used in developing and improving the care for ALS patients and their relatives as well as helping healthcare professionals who perform the care. There are few longitudinal and prospective studies with newly diagnosed ALS patients that have investigated quality of life, coping strategies and emotional well-being. The review of the literature shows that several studies have been conducted on the topics regarding quality of life, coping and emotional well-being among ALS patients, but most of those studies were performed at one time point and often with patients in different stages of the disease. However, to our knowledge there are very few, if any, studies that have evaluated these topics among newly diagnosed ALS patients over time.

In 1999, I started my work as the coordinating nurse in the ALS team at the Neurological ward, Uppsala University hospital. Since then, I have followed patients and relatives from diagnosis and during the disease progression, and I have often wondered how patients manage to live with such a devastating disease. How does the disease influence their quality of life and emotional well-being? How do they cope with the disease? Most often, it is the relatives who are involved in the care. Without any education in healthcare or specific knowledge about the disease, they are expected to manage the situation. Due to these questions, we started this multi-centred study in 2009 with focus on quality of life, coping and emotional well-being among newly diagnosed ALS patients during the disease progression. An additional focus was the relatives’ experience of the care and the support they require themselves.
Background

ALS

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder, where the motor neurons responsible for controlling the voluntary muscles are affected (1). Due to the variety of clinical features in the early stages of ALS and the absence of a definite diagnostic test for ALS, it is difficult to make an absolute diagnosis. The diagnosis of ALS is made on clinical grounds, using internationally set criteria, after exclusion of conditions that can mimic ALS. In 1994, the World Federation of Neurology developed the El Escorial criteria for diagnosis of ALS (2), which was revised in 1999 (3). The criteria for the diagnosis is presence of both upper- and lower motor neuron degeneration, progressive spread of symptoms or signs within a region or to other regions, together with absence of electrophysiological and neuroimaging evidence of other diseases that might explain the symptoms and signs. Based on clinical findings, ALS is categorised into: Definite ALS, Probable ALS or Possible ALS (3). Most cases, 90–95%, are classified as sporadic ALS (SALS) (i.e. without genetic component) and 5–10% as familiar ALS (FALS) (i.e. with a positive family history) (4). Independent of classification, the disease leads to similar symptoms with similar need for support and care during the disease progression.

The cause of ALS is unknown, but several hypotheses about the pathogenesis (1, 5) have been suggested, ranging from genetic factors (6, 7), excitotoxicity (8, 9), oxidative stress (10), programmed cell death (11), nerve growth factors (12), protein aggregation (13) and exogenous causes (14). ALS is probably a multi-factorial and multi-systemic disease, which may explain the difficulties in solving the mystery of the cause of the disease (15, 16).

The incidence of ALS in Europe is 2.16 per 100,000 persons per year, and the incidence is higher among men than women (17). The incidence of ALS has generally increased during the last few years.

The disease often starts at 55–70 years of age, but can be seen at the age of 20 (18). Due to the characteristics of the disease, with death of both upper- and lower motor neurons, the patient will gradually develop muscle atrophy and weakness. Most often, the disease starts with weakness in one arm or leg “i.e. limb onset”, but the disease can also start with speech and/or swallowing difficulties “i.e. bulbar onset”. The muscle weakness also affects
the respiratory muscles, which leads to respiratory insufficiency (19). During the disease progression, the patient has to face different changes that affect him or her physically, socially and psychologically; moreover, the symptoms often lead to dependence on others and changes in life style (20, 21). Studies have shown that cognitive impairment is more common than expected among patients with ALS, and that 5–10 % of the patients develop frontotemporal dementia (22, 23). The patients’ cognitive impairment develops into a language dysfunction that is most obvious when the patient communicates in writing, with difficulties forming sentences and using correct spelling. Despite this language dysfunction, the patients’ general intellectual abilities seem to be unaffected (24).

Median survival from onset of symptoms range between 2–5 years, and the most common cause of death is respiratory failure, depending on the respiratory muscle weakness (15, 18). Five to 10 per cent of ALS patients survive for more than 10 years. Several prognostic factors have been identified as being important for survival with ALS (25, 26). Age of onset is related to the patients’ survival (27); younger patients (younger than 50 years of age at initial visit) have a better survival rate than older patients. The site of onset is also a determining factor, where bulbar onset of the disease is associated with a worsened prognosis than limb onset (28); low body mass index (BMI) at diagnosis (29) and respiratory status, with low forced vital capacity (FVC) are negative prognostic factors for survival (30).

There is no known cure for ALS today, and the only neuroprotective drug approved for ALS is Riluzole, which prolongs life by 2–3 months (31-33). Even if the disease is incurable, many of the symptoms caused by the disease can be treated effectively (22, 34-36).

The relatives

Relatives are often central in caring for patients with ALS. Caring for a family member with ALS may involve considerable physical, emotional and social challenges; furthermore, being close to someone with ALS may be enormously stressful for the family members and friends. Relatives often assist the patient with personal care, communicating with others, providing medications, moving and transferring (20, 37), and most relatives dedicate many hours every day to help the patient with daily activities (38). This can lead to fewer social contacts for the relatives; moreover, their ability to take part in leisure time activities decreases (21). The emotional burden depends on factors such as knowing that your loved one is dying and having to watch the patient suffer (39). Factors such as number of hours dedicated to providing assistance, physical well-being and feeling of lost opportunities also add to the burden felt by relatives of ALS patients (40). The burden increases as the disease progresses (40-42), and the care may have a negative influence
on both one’s physical health and emotional well-being (43). To take part in palliative care does not only mean negative feelings, it also mean positive feelings, that is, feelings of being helpful, being there for a loved one and bringing some happiness, which can be rewarding to relatives who participate in the care (39, 44).

Due to the disease progression, health professionals have to plan the caring actions in advance, which can be difficult for both patients and relatives who aim to live in the present and have difficulty thinking about the future (45). Caring for a terminally ill relative is stressful; thus, relatives need support from health professionals who understand their situation. However, limitations of support from former health professionals are a source of stress for caregivers (46, 47). The need for support varies during the course of the disease, from need for information to being able to be with their sick relative or taking part in the care. Relatives often rely on family, friends and neighbours to handle the stressful effects of caregiving (46). Caring for patients with a neurological disease may lead to restricted social life and decreased activities (47), and due to the disease progression and the patients’ physical limitations relative’s lives become more centred around the home (48). It has been shown that most relatives do not have time to think about their own situation; instead, they keep busy and just keep on going (49). By focusing on the disease and the patient’s needs, relatives take control over the situation (50). In a study by Martin and Turbull (2001), it was found that a majority of the relatives of ALS patients’ felt burnt out after the patients had died (51).

The care

Since there is no known cure for ALS today, the palliative care starts as soon as the patient receives the diagnosis. The National Board of Health and Welfare in Sweden define palliative care as care with the aim to prevent and relieve suffering and to enhance quality of life among patients with a progressive, incurable disease or injury, including care for their families (52). This definition is in line with the definition given by the World Health Organisation (WHO) (53). Palliative care has characteristics of a holistic approach with the aim to support the individual to live with dignity and as great well-being as possible to the end of life. The four keystones in palliative care are (54):

- Symptom relief (including physical, psychological, social and existential needs)
- Multi-professional collaboration
- Communication and relation (within and between team and the relationship to patients and relatives)
• Support for relatives (to be invited to take part in care and to receive support during the disease progression as well as after the patient has passed away).

In Sweden, neurology clinics at the university hospitals and regional hospitals have a specialised ALS team responsible for caring for ALS patients and their relatives. The aims of the team are to meet the physical, psychological, social and existential problems that arise during the disease progression. In addition to the specialised ALS care, care should also include a palliative care team. The aims of the ALS team and the palliative care team do not differ; the purpose of the care is to relieve symptoms and to provide emotional support, with the goal to achieve the best possible quality of life during the disease progression. The differences may be due to resources; the palliative care team in Sweden is available 24 hours, 7 days a week and make house calls, in contrast to the ALS team who work office hours and meet the patients at the hospital. Early cooperation between the teams is important for both patients and families (55).

Since ALS is a progressive disease with increasing disabilities, it is essential to detect it early on, carefully analyse and treat physical, psychological, social and existential problems that occur during the disease progression in collaboration with a multi-professional team (52). Depending on the different symptoms caused by the disease, the patient needs different kinds of aid and support during the disease duration. There are no national guidelines for ALS care in Sweden at present, but international evidenced-based guidelines that help clinicians to treat, help and provide support have been developed (56, 57). These guidelines help the team to set goals for the patient’s care.

The management style to care for ALS patient is supportive, palliative and multi-disciplinary. Studies have shown that multi-disciplinary team has important role in providing care for ALS patients (58-60). This team should include a neurologist, nurse, social worker, physiotherapist, occupational therapist, speech therapist and dietician; furthermore, the recommendation is that patients have scheduled clinical visits every two to three months (34). The care should have holistic approach and have the whole patient in focus, with the aim to meet the physical, psychological, social and practical problems that arise during disease progression. Another important aim is to help the patient and relatives to retain as good quality of life as possible (19, 34). Due to the disease progression, the aid and support must be provided immediately when the patient needs it; otherwise, it can be too late. Accordingly, demands are placed on different team members in order to avoid unnecessary delays for the patient, for example, getting the equipment needed such as lifting devices or electric wheelchairs, which can take some time to be delivered. Health professionals’ knowledge and understanding of the disease and how the disease affects the patients and relatives’ situation are important factors in providing the best care (21, 61). It can be a difficult balance, on
the one hand, doing the right thing and enough, and on the other hand, not taking the control away from the patient and relative. Even though it is of great importance to support and help the patients, it is also important to respect them and help them to maintain their autonomy (62). The physical changes and losses due to the disease have impact on both patients and relatives’ daily living, and they have to struggle to regain some sense of normalcy. By letting them handle things they can do for themselves, the health professionals help patients and relatives to gain some control over their situation (63).

Quality of life

Quality of life (QoL) may be difficult to define, but most individuals associate QoL with life satisfaction and well-being. The World Health Organisation (WHO) defines QoL as ‘individuals perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns’ (64). QoL is subjective and multi-dimensional, including both positive and negative aspects of the physical, psychological, social and spiritual dimensions of QoL (65). It is also dynamic, meaning that values and self-evaluation of life may change over time in response to life, health events and experiences (66). A person’s QoL depends on several factors such as: past experience, present lifestyles, hope and ambition for the future (67). People value different aspects of life, and the meaning of QoL means different things for different people (68). Due to the fact that QoL is subjective, the individual him or herself is the best judge of their own QoL. The concept of QoL is important in both research and clinical practice to evaluate treatment and quality of care, especially among patients with a progressive disease (69). To evaluate QoL in medicine and health care, different methodologies have been used, focusing on health related quality of life or individual quality of life.

Health-related quality of life

In health-related quality of life (HRQoL), the physical and social impact that the disease and treatment may have on the patient’s daily life is evaluated (66). HRQoL can be described as the discrepancy between the individual’s expectations and experience of health. Meaning that if the person’s expectations match the experience there is no impact on the QoL, but if the experience of health is worse than expectations there will be an impact (68). HRQoL is often measured with standardised generic or disease-specific questionnaires with focus on functional status rather than subjective perceptions of QoL. Generic questionnaires measure aspect of importance for eve-
ryone, in contrast to disease-specific questionnaires which are designed for a specific patient group (66).

Individual quality of life
The individual quality of life (iQoL) focuses on the patient’s own perspective of QoL based on areas in life that the individual considers to be important for him or her at the present time (70). Perception of QoL may vary between individuals. What is important for one individual may have little or no relevance to another individual (67). One instrument that often is used to study iQoL among ALS patients is the Schedule of the Evaluation of Quality of Life-Direct Weighting (SEIQoL-DW). This instrument allows the patient to nominate areas that are important for his or her QoL, assess the level of functioning and the relative importance for each area (70).

Quality of life among ALS patients
Most often, both HRQoL and instrument measuring iQoL have been used when studying QoL among ALS patients. Studies have shown that physical function in ALS is not important in determining QoL, but that psychological and existential issues, social support and spirituality are important for the overall QoL (60, 71). Other areas of importance are family (72, 73), friends and profession (74). Olsson et al. (2010) found that patients rated their HRQoL poorer than the general Swedish population and that their HRQoL changed over time (75). The iQoL, on the other hand, remained stable over time (76), which is in agreement with several other studies (77, 78). In a study by Lulé et al. (2013), it was shown that health professionals rated the patients’ QoL as being lower than the patients themselves (79). This highlights the fact that QoL is individually based and that health providers need to evaluate the patients’ QoL and not try to determine it based on their own expectations and experiences. Despite the fact that most studies have shown that physical function is not relevant for QoL in ALS patients, health is often mentioned as an important area for their iQoL (72, 73, 76). Several studies have shown that patients with ALS estimate their QoL as good (60, 74, 80, 81), and Fegg et al. (2005) found that ALS patients rated their QoL higher compared with patients with advanced cancer (82).

Coping
Stress can be described as result of the disturbance in the interplay between the demands an individual experiences and the resources he or she experiences to have at his or her disposal to manage the demands. Different strategies need to be used to handle the stress. Coping can be described as ‘a pro-
cess by which the individual tries to manage the perceived discrepancy between the demands and the resources they appraise in a stressful situation’ (83). The coping process includes both cognitive and behavioural activities; the process must be weaved in its actual context, and the coping strategies are part of the process and not reflective of the results (84). Coping included attempts to reduce the perceived discrepancy between situational demands and personal resources (85). Lazarus and Folkman (1984) define coping as ‘constantly changing cognitive and behavioral efforts to manage specific external and internal demands that are appraised as taxing or exceeding the resources of the person’ (84).

Lazarus and Folkman’s appraisal theory of coping includes:

- Identification of the stressful situation
- Appraisal of the stressful situation
- Coping with the stressful situation
- And outcome of the situation.

The theory describes two types of appraisal: primary appraisal (the individual’s evaluation of the situation) and secondary appraisal (the individual’s evaluation of his/her ability to handle the situation). Lazarus and Folkman (1984) describe two functions of coping: problem-focused coping and emotion-focused coping. Problem-focused coping aims to modify sources of the stressor, and emotion-focused coping aims to reduce or manage emotional stress that is associated with the situation. This function of coping should not be viewed as two independent types of coping, instead they complement each other in the coping process (84). In the revised model of Lazarus and Folkman’s coping theory, a third function of coping is described: the meaning-based coping which includes positive reappraisal. In meaning-based coping, the individual, by using cognitive strategies, reframes a stressful situation and focuses on positive aspects, benefits or potentially positive interpretations of a negative situation (86). Most individuals often use different strategies in stressful situations depending on the complexity of the situation, having to handle several threats (87, 88). Studies have shown that coping strategies influence QoL in patients with neurological diseases (89-93).

**Coping with ALS**

In ALS, the patient has to cope with threats such as loss of physical ability leading to dependence on others, changed social life and the knowledge of living with a fatal disease. The complexity of losses as a consequence of ALS may lead to stress; thus, to be able to cope with the stress, patients have to adopt strategies that help them to make the situation manageable. There seems to be a difference between age groups in use of coping strategies; younger ALS patients often use problem-focused strategies, whereas older
patients often use emotion-focused strategies to cope with the disease (88). Optimism, flexibility and humour are found to be important strategies that many ALS patients use to cope with their situation. Moreover, spirituality and religious practice such as prayer, medication and believing in God are important sources of support in coping with ALS (90). Montel et al. (2012) found that the most common strategy was acceptance. They also found that ALS patients used religion more often to cope than the general population and that woman tended to look for emotional support more often than men (94). Often people use avoidance to deal with stress in order to get away from the source of stress. Studies have shown that avoidance is one of the most commonly used coping strategies to handle stress among patients with a neurological illness (95, 96). When such strategy is effective, it may improve the patient’s emotional state, but it can also be negative if it takes attention away from a problem that needs to be solved (97).

ALS is a progressive disorder; accordingly, patients will require different coping strategies at different stages of the disease (88, 98). A study by Tramonti et al. (2012) showed that patients with less influence on their physical ability more often used independence to cope; however, when their physical function decreased, the use of independence as a way of coping also decreased. Their study also showed that use of positive action and support emerged during the disease progression (62). This review of studies show that ALS patients use both problem-focused and emotion-focused strategies to cope with the disease, and that there is a variety in the use of strategies over time. This may depend on the situational complexity, where there are several threats to handle and changed circumstances depending on the disease progression (84).

Emotional well-being

To be diagnosed with a life-threatening illness such as ALS threatens one’s personal existence and security, which can lead to a traumatic crisis for the patient. ALS involves handling different losses and consequences of the disease during the disease progression. Normally, most individuals manage to handle these changes with support from family and friends, but psychologically painful losses can lead to depression and/or anxiety symptoms. Depression and anxiety can be triggered by losses that are important for the person’s self-esteem. Most often, this is an adequate reaction and the patient learns to handle these life situations, but sometimes he/she needs help to manage them (99).

Different factors such as physical, psychological, psychosocial symptoms and existential distress contribute to emotional distress among ALS patients (100). Most findings in research indicate that clinically significant depression and anxiety are not as present or as severe as might be expected in ALS.
patients due to impact on physical function or severity of the disease (37, 101-103), even if ALS patients score higher than norms for adults (101, 104). In contrast, other studies have shown that emotional distress is common among ALS patients (105, 106). Prevalence of depression may be higher following diagnosis but decreases over time. It is not unusual that patients with ALS undergo a phase of reactive depression soon after diagnosis (107, 108), which may be one explanation (109). It seems that depression does not increase late in the disease (110-112). However, there is still lack of knowledge about the real prevalence of anxiety and depression among ALS patients (102).

Patients with bulbar impairment, leading to speech- and/or swallowing difficulties, suffered more from depression and anxiety than patients with limb impairment (110-112). There is no or little correlation between depression or anxiety and the patients’ physical function (102, 106, 113) or illness progression (106, 114). The psychological health affects many different areas and is important for the patient’s quality of life and coping ability (115). Psychological well-being is related to survival time in ALS, with significantly higher median time for survival among patients with low scores on depression and anxiety (25, 109). Anxiety and depression are more common among patients that are old at disease onset (116). The desire to hasten death in end-stage disease can be sign of depression (117). Because of this impact on the patient’s life, it is important to assess for depression and anxiety on a routine basis, and to ensure that patients receive treatment if necessary. A greater duration of time between symptom onset and time before diagnosis of ALS increases risk for depressive symptoms (118). Depressive symptoms have negative effect on patient’s ability to accept help and support (117).

Rationale for the study

This thesis examines QoL, coping and emotional well-being both prospectively and longitudinally among newly diagnosed ALS patients. There are few studies that have examined these topics among ALS patients from longitudinal perspective and even fewer with newly diagnosed patients. Additional aim was to investigate how relatives experience the care for the patients and the support they received themselves during the disease progression. By identifying the patients’ perspective of QoL, strategies used to cope with the disease and the relatives’ experience of the care and support, it will be easier to identify and prioritise problems that are of importance for the patient and relatives and to better meet their needs. Present study has hopefully provided deeper knowledge and understanding, which can be used in clinical practice and to develop and improve the care for ALS patients and their relatives in Sweden during the disease progression.
Aims

Overall aim of this present thesis was to investigate quality of life, coping and emotional distress (i.e. anxiety and depression) among newly diagnosed ALS patients. Additional aim was to investigate how relatives experience the care for the patient and the support they received for themselves during the disease progression. Specific aims were:

I  To prospectively identify areas of importance for the individual quality of life among ALS patients, from diagnosis and during the disease progression. Specifically, how the patients evaluate their QoL, if there were any changes in their perceived QoL and if QoL correlated with physical function or emotional well-being.

II  To prospectively identify what coping strategies ALS patients use from diagnosis to six months after diagnosis and whether their coping strategies changed over time. Additional aim was to investigate coping, on the one hand, and emotional distress and physical function, on the other hand, and to determine whether there were differences between gender and age groups with respect to coping strategies used at the two time points.

III  To evaluate which specific coping strategies patients with ALS use and if there were any differences from early stage and over time. Secondly, if there was a correlation between the use of different coping strategies, emotional well-being and physical function from diagnosis and during the disease progression.

IV  To describe how relatives experienced the care for the patient and the support they received for themselves.
Material and methods

Study design
This thesis consists of four clinical studies: three with patients and one with relatives. Both quantitative and qualitative methods were used. An overview of the studies is shown in Table 1. Study I was prospective, longitudinal, descriptive and comparative. Study II and III were prospective, longitudinal and descriptive. Study IV was descriptive, with a qualitative method for data collection and analysis.

Table 1. Overview of the studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample</th>
<th>Examination interval</th>
<th>Data Collection</th>
<th>Data analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>36 patients</td>
<td>1-3 months after diagnosis and then 6, 12, 18 and 24 months after diagnosis</td>
<td>Questionnaires: HADS, SEIQoL-DW, ALS FRS-R</td>
<td>Descriptive statistics, Linear Mixt Model, Spearman’s rho</td>
</tr>
<tr>
<td>II</td>
<td>33 patients</td>
<td>1-3 months after diagnosis and then six months after diagnosis</td>
<td>Questionnaires: HADS, MNDCS, ALS FRS-R</td>
<td>Descriptive statistics, Spearman’s rho, Mann-Whitney U test, Wilcoxon sign-rank</td>
</tr>
<tr>
<td>III</td>
<td>36 patients</td>
<td>1-3 months after diagnosis and then 6, 12, 18 and 24 months after diagnosis</td>
<td>Questionnaires: HADS, MNDCS, ALS FRS-R</td>
<td>Descriptive statistics, Spearman’s rho</td>
</tr>
<tr>
<td>IV</td>
<td>15 relatives</td>
<td>6-12 months after the patient had died</td>
<td>Interview with a semi-structured interview guide</td>
<td>Descriptive statistics, Qualitative content analysis</td>
</tr>
</tbody>
</table>

Setting
Data collection for studies I, II and III was conducted by means of home visits one to three months after diagnosis and then every six months during period of two years. On two individual occasions, data collection was conducted in connection with regular visit with the team. In study IV, the data collection was conducted by home visits, within six to twelve months after the patient had died.
Subjects

All newly diagnosed ALS patients cared for by the ALS team from the hospitals in Uppsala, Eskilstuna and Västerås from July 2009 to October 2011 who met the criteria for a diagnosis of definite or probable ALS, according to the El Escorial criteria (3), were asked to participate in studies I, II and III. The patients had to be 20 years or older and be able to understand and express themselves in the Swedish language. Patients with hereditary motor neuron disease (familial ALS (FALS), Kennedys syndrome and hereditary spinal muscle atrophy (SMA)), other serious diseases or dementia were excluded. The number of participants at each time point for each study is shown in Table 2.

Table 2. The number of patients at each time point.

<table>
<thead>
<tr>
<th></th>
<th>TP1</th>
<th>TP2</th>
<th>TP3</th>
<th>TP4</th>
<th>TP5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies I+III</td>
<td>34</td>
<td>31</td>
<td>24</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>Study II</td>
<td>31</td>
<td>28</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TP1 = 1-3 months after diagnosis, TP 2 = after 6 months, TP 3 = after 12 months, TP 4 = after 18 months and TP 5 = after 24 months.

For study IV, relatives from two different neurology departments with multidisciplinary teams were recruited. Relatives refer to husband, wife, significant other and children. Relatives had to be 18 years of age or older and be able to understand and express themselves in the Swedish language. Relatives with cognitive affection or dementia were not included in the study. Those relatives included in study IV are not related to patients in studies I, II or III. A convenient sampling was used to recruit the relatives.

Studies I, II & III

A total of 60 patients fulfilled the inclusion criteria. Two patients died shortly after diagnosis and 15 patients were excluded: two due to other fatal diseases, eight due to psychological distress and two due to severe symptoms of ALS. One patient was excluded due to changed diagnosis, and two patients were excluded due to administrative failure. Seven patients declined participation in the study. A total of 36 patients finally participated in the studies I and III and 33 patients in study II. Two patients were included more than four months after being diagnosed and were therefore excluded at time point 1, but included at time point 2. Overview of the characteristics is shown in Table 3.
Table 3. The characteristics of the patients at baseline.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age Mean ± SD (range)</th>
<th>Onset</th>
<th>Education ≤ 9</th>
<th>&gt; 9 (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Limb</td>
<td>Bulbar</td>
</tr>
<tr>
<td>Studies I + III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female  (n = 16)</td>
<td>60.2 ± 13.2 (35 - 77)</td>
<td>11</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Male    (n = 20)</td>
<td>68.7 ± 10.0 (54 - 88)</td>
<td>17</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Study II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female  (n = 14)</td>
<td>58.5 ± 13.2 (35 - 77)</td>
<td>10</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Male    (n = 19)</td>
<td>69.2 ± 10.1 (54 - 88)</td>
<td>17</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

Study IV

Relatives were contacted by letter with written information about the study, including purpose of the study, voluntary nature of participation, procedure for data collection, confidentiality and a form to sign for informed consent. The letter also included a stamped return envelope. A total of 25 relatives were contacted; of those, two relatives declined participation, six relatives did not answer the request and two relatives could not be included due to practical issues. When the relative had agreed to participate, the researcher called the relative and gave verbal information about the study and booked a time for interview. Finally, a total of 15 relatives consented to participate in the study. Overview of the characteristics is shown in Table 4. Thirteen of the relatives had been involved in the care on full time basis, one a few hours and one had not been involved in the practical care. The relatives were interviewed 6-12 months after the patients had died.

Table 4. Characteristics of the relatives, study IV.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age Mean ± SD (range)</th>
<th>Education ≤ 9</th>
<th>&gt; 9 (years)</th>
<th>Relation spouses</th>
<th>children Yes</th>
<th>No</th>
<th>Involved in care (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (n=11)</td>
<td>50.0 ± 17.7 (26-79)</td>
<td>2</td>
<td>9</td>
<td>7</td>
<td>4</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Male (n=4)</td>
<td>64.0 ± 3.2 (61-68)</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>
Data collection

Data were collected by both quantitative and qualitative methods. The studies were accomplished by questionnaires and interviews (Table 1).

ALS FRS-R

To estimate the patient’s degree of physical impairment, the revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALS FRS-R) was used (119). This scale consists of 12 questions where the patient’s physical function, breathing and speech- and swallowing ability were graded from 0 = total loss to 4 = normal function, with a maximum score of 48 points. Lower score indicates a higher level of dysfunction. The internal consistency for bulbar function, fine/gross motor task and respiratory function was assessed using Cronbach’s alpha. Coefficient > 0.70 is suggested to reflect good internal consistency of the instrument (120). The value for each domain from the current sample at time point 1 was 0.90 for bulbar function, 0.83 for fine/gross motor tasks and 0.84 for respiratory function.

HADS

The Hospital Anxiety and Depression Scale (HADS) measures the presence and severity of depression and anxiety over the past week and consists of two sub-scales: one for anxiety (7 items) and one for depression (7 items). All questions were rated on a 4-level scale (0-3 points), and each subscale score ranged from 0 (no distress) to 21 (maximum distress) (121). The HADS-scale is well validated for use in detecting anxiety and depression in somatically ill patients (122, 123). According to standardised cut-offs on respective sub-scales, patients scoring above 11 are considered to be clinically depressed or anxious. The internal consistency for anxiety and depression was assessed using Cronbach’s alpha. The value for each sub-scale from current sample was 0.80 for HAD anxiety and for 0.67 for HAD depression at time point 1. The HADS was supplemented with questions about treatment for depression and anxiety. The HADS has been evaluated in a Swedish population sample, and was considered as useful clinical indicator for clinical anxiety and depression(124).

SEIQoL-DW

To evaluate quality of life, the Schedule of Evaluation of Individual Quality of Life- Direct Weighting (SEIQoL-DW) was used, which is an interview-based instrument (70). This instrument has been used with a variety of patient groups. First, the respondents are asked to nominate five most important areas of their life at present time (cue). The interviewer wrote down
the answers directly on a cue definitions record form. It is important to doc-
ument the definition for each cue given by the respondent to be able to un-
derstand what the respondent means by each area. Secondly, the patients
were asked to rate their current level for each of the nominated cue on a vis-
ual analogue scale (VAS) from 0–100. At the third stage, the patients deter-
mined the relative importance of each cue by direct weighting, using a col-
oured disc. The disc is graded from 0–100; a more important area is given a
larger area and a less important area a smaller area of the disc.

The MNS Coping Scale

The Motor Neuron Disease Coping Scale (MNDCS) is a disease specific
instrument developed to measure coping strategies in people with ALS
(125). It consists of 18-items divided into six domains: support, 4-items;
positive action, 3-items; independence, 4-items; avoidance/venting, 3-items;
information-seeking, 2-items and positive thinking, 2-items. The scale also
comprises four single items; item 15 ‘I am philosophical about my illness,
whatever will be will be’; item 18 ‘I keep my feelings from my friends and
family’; item 19 ‘I make use of alternative/complimentary therapies’, and
item 20 ‘I take comfort in my spiritual/religious beliefs’. All items are scored
on a 6-point likert scale, with the purpose of describing the extent to which
the patient uses each coping strategy. The scale has been found to be reliable
and valid. The questionnaire was translated into Swedish by a translator and
tested on eight patients with ALS before it was used in the present study.
The questionnaire was sent out to 16 patients, with the purpose to evaluate if
the patients felt that the statement was relevant and if they experienced any
difficulties when filling out the form. A total of 13 patients completed the
questionnaire; a majority of the patients answered that they felt the statement
to be relevant and that it was easy to fill out the form. The internal con-
sistency for each strategy was assessed using Cronbach’s alpha at time point
1. The value for Support was 0.26, Positive action 0.41, Independence 0.51,
Avoidance/venting -0.23, Information seeking 0.50 and Positive thinking
0.46.

Qualitative interview

Since the aim was to describe how relatives experienced the care for the
patient and support they received for themselves from their own perspective,
a qualitative interview was deemed to be the best method to obtain
knowledge (126). To guarantee that all relatives were asked the same ques-
tions, a semi-structured interview guide was used. By using open-ended
questions, the interviewer allowed the participants to freely express their
experiences in their own terms (127).
Demographic data
The demographic data were collected with help of a questionnaire with questions about gender, age, relation, education and onset of disease. For study IV, one question about involvement in the patient’s care was added.

Study I
Data were collected with questionnaires. Individual QoL was measured with the SEIQoL-DW (70), and depression and anxiety were measured using the Hospital Anxiety and Depression Scale (HADS) (121). The patients were interviewed at five time points: 1–3 months, 6, 12, 18 and 24 months after diagnosis. Patients who had difficulties in completing the HADS received help from the data collection researcher. The patients’ physical function was estimated with the ALS FRS-R (119), which was completed by the data collection researcher. All data collection was conducted privately with each participant.

Study II & III
Data were collected with questionnaires. The patients’ coping strategies were measured with the MND Coping Scale (MNDCS) (125), and anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS) (121). In study II the patients filled out the questionnaires at two time points: 1–3 months and 6 months after diagnosis. In study III the patients filled out the questionnaires at five time points: 1–3 months and 6, 12, 18 and 24 months after diagnosis. Patients who had difficulties in completing the questionnaires received help from the data collection researcher. The patients’ physical function was estimated with the ALS FRS-R (119), which was completed by the data collection researcher.

Study IV
Data were collected through face-to-face interviews in the participants’ home 6–12 months after the patient had died. The interviews were conducted by the data collection researcher and were audio recorded, and clarifying notes were taken during the interviews. The time for the interviews varied between 10 to 56 minutes, and to guarantee that all participants answered the same questions an interview guide was used. First, the participants were asked to describe the care that their sick relative received during the disease duration, their experience of the care and what they felt when they thought of the care. Secondly, the participants were asked to describe the support they received for themselves, their experience of the support and what they felt when they thought about the support they received for themselves during
the disease duration. Follow-up questions were asked to clarify and to get a deeper understanding of the topics.

Analyses

Descriptive statistics were used to describe the demographic characteristics of the participants in the studies.

Study I

Descriptive statistics were used to describe the demographic and clinical characteristics of the participants and are presented as frequencies, means with standard deviations (SD) and range. The answers to the questions in the SEIQoL-DW were written down directly during the interview. The nominated cues were then grouped into areas, based on the cue label and definition the respondent used to describe each cue. The data analytic process involved a back-and-forth interchange until the authors agreed on 17 areas of importance for the quality of life among the patients. The content in each area was described qualitatively. Analyses of the development of SEIQoL-DW index and the other scales over time were conducted using linear mixed model, with time as a continuous fixed variable, with corresponding 95% confidence interval. Spearman’s rho was used to analyse if the SEIQoL-DW index correlated with the ALS FRS-R or the HADS. P-value was not adjusted for number of tests. Due to the multiple tests performed, a P-value of < 0.01 was considered significant. SPSS, version 17, (SPSS Inc. Chicago, IL, USA) was used for statistical analysis.

Study II

To describe the demographic data and clinical characteristics of the sample, descriptive statistics were used. Since the data were of ordinal level and we could not assume the data to be on normal distribution, nonparametric tests were used to analyse the data. The Spearman’s rho (r_s) was used to analyse the correlation between HADS, ALS FRS-R and the MNDCS. To analyse differences in coping strategies between gender as well as between age groups (i.e. ≤ 64 years and ≥ 65 years), Mann-Whitney U test was used. To analyse whether there were any differences between the two time points, Wilcoxon signed-rank test was used. Significance level was p = 0.05 (two-tailed). The focus was on the presence, correlation and change over time when the results were presented. For statistical analysis, the SPSS, version 17 (SPSS Inc. Chicago, IL, USA) was used.
Study III
To describe the demographic and clinical characteristics, descriptive statistics were used. Continuous variables are described as mean and standard variation and categorical as absolute and relative frequencies. Correlation between coping strategies, ALS FRS-R, anxiety and depression were analysed using Spearman’s rho. P-values were unadjusted and should thus be interpreted conservatively. For the statistical analysis, we used SPSS version 17, (SPSS Inc. Chicago, IL, USA) and R version 3.1.1.

Study IV
To describe the demographic data, descriptive statistics were used. The first author (BJL) transcribed the interviews verbatim. Since the first author had been involved in the care of some of the patients, the second author (CF) double-checked eight (four from each participating teams) randomly selected transcribed texts against the audio-tapes, with the purpose of detecting if there were any differences in the interviewer’s behaviour towards the relatives known to her compared to those she had not met previously. No difference was detected. The interviews were analysed using content analysis (126, 128) and were performed by two of the authors (BJL and CF). The interviews were divided into two content areas: 1) how the relatives experienced the care for the patients and 2) their experience of the support they received for themselves during the disease progression.

The analysis consists of several steps:

1. The interviews were transcribed verbatim.
2. The interviews were read and re-read several times to get a sense of the whole and to become familiar with the individual interviews.
3. Meaning units, related to the aim for each content area, were identified.
4. The meaning units were condensed, and each meaning unit was then labeled with a code on the basis of its content.
5. The codes were interpreted, compared and sorted for similarities and differences, and categories were developed based on the codes.
6. Finally, the categories were sorted and abstracted, and a theme for each content area was formulated due to the latent content of the interviews.
This analytical process involved a back and forth movement between the whole and the parts of the texts until the authors reached agreement in meaning units, codes, categories and themes.

**Ethical and methodical considerations**

Approval for the study was granted by the Regional Ethics Review Board in Uppsala, Sweden (Dnr.2009/007). The participants received both oral and written information about the purpose of the study, the voluntary nature of participation, being free to withdraw at any time and that confidentiality was guaranteed. Written consent was obtained from all participants before the study started. The ethical question in this study related to whether there was any risk that the participants could be harmed by answering questions on physical function, emotional well-being, coping or quality of life. The researcher must be perceptive and take into consideration that feelings of sorrow and grief may aroused when asking patients with a progressive and fatal disease such questions. The same consideration must also be taken when asking relatives of deceased patients about their experiences of the care for the patient and support for themselves. Therefore, we had prepared for readily available support if it was needed; however, none of the participants used that support.
Results

Study I
The cues mentioned by the patients were grouped into 17 areas based on the cue label and the description for each cue used by the patients.

Areas of importance for QoL
The areas mentioned were: marriage, family, friends, own physical health, own mental health, health among relatives, independence, support/aid, social activities, sport/exercise, hobbies, outdoor activities, work, finances, living and pets. Areas such as marriage, family and own physical health were shown to be of great importance for the patients overall QoL during the disease progression. Relations with others such as family and friends were the most frequently mentioned areas at all-time points (Figure 1).

Figure 1. Percentage for each nominated area at the different time points.
These areas included descriptions such as feelings of fellowship and social interactions with others. It was important to be supported and helped by family and friends, but also being able to support the family too. Furthermore, one’s own physical health was often mentioned as an important area for the individual QoL. This area included functions of importance for their daily living such as mobility, eating, writing, speech, sleep, strength and energy.

QoL index and changes over time

The SEIQoL-DW index showed that most patients rated their QoL as relatively good, and the SEIQoL-DW index remained stable during the disease progression (Table 5). Even though most patients rated their QoL as being good, there were some patients with scores indicating a poor QoL. There was a fluctuation in QoL among those patients over time (data not shown). Areas such as own physical function, outdoor activities and social activities were often mentioned at those times with low cue levels but given high cue weight (data not shown). This indicated that those areas functioned poorly, but were still considered as being important for their QoL.

Table 5. Mean and median score for the SEIQoL-DW from baseline and over time.

<table>
<thead>
<tr>
<th></th>
<th>TP1 (n = 34)</th>
<th>TP2 (n = 31)</th>
<th>TP3 (n = 24)</th>
<th>TP4 (n = 16)</th>
<th>TP5 (n = 12)</th>
<th>Changes over time</th>
</tr>
</thead>
<tbody>
<tr>
<td>QoL-index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>68.1 (18.5)</td>
<td>67.1 (22.2)</td>
<td>68.3 (23.6)</td>
<td>64.7 (24.9)</td>
<td>77.2 (15.8)</td>
<td>p = 0.598</td>
</tr>
<tr>
<td>Median</td>
<td>70.1</td>
<td>74.0</td>
<td>77.0</td>
<td>70.3</td>
<td>78.3</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>16-93</td>
<td>6-93</td>
<td>13-100</td>
<td>7-96</td>
<td>49-96</td>
<td></td>
</tr>
</tbody>
</table>

Physical function and emotional well-being

The mean score on the ALS FRS-R decreased over time, with a significant increase in function disabilities. There was a significant change in anxiety but not in depression over time (Table 6). A total of eight patients scored above the cut-off for clinical anxiety and/or depression on the HADS during the first year after diagnosis (data not shown).
**Table 6. Mean scores for ALS FRS-R and HADS subscales over time.**

<table>
<thead>
<tr>
<th></th>
<th>TP1</th>
<th>TP2</th>
<th>TP3</th>
<th>TP4</th>
<th>TP5</th>
<th>Change over time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALS FRS-R</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>37.6 (6.4)</td>
<td>33.1 (9.8)</td>
<td>29.7 (9.1)</td>
<td>26.4 (12.0)</td>
<td>26.2 (12.4)</td>
<td>p = 0.001</td>
</tr>
<tr>
<td>median</td>
<td>38.0</td>
<td>35.0</td>
<td>30.5</td>
<td>25.0</td>
<td>23.5</td>
<td></td>
</tr>
<tr>
<td>range</td>
<td>23-46</td>
<td>10-46</td>
<td>7-46</td>
<td>4-46</td>
<td>5-46</td>
<td></td>
</tr>
<tr>
<td><strong>HADSa</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>6.3 (3.5)</td>
<td>5.3 (3.1)</td>
<td>4.3 (2.7)</td>
<td>3.6 (2.5)</td>
<td>3.4 (3.0)</td>
<td>p = 0.002</td>
</tr>
<tr>
<td>median</td>
<td>6.0</td>
<td>5.0</td>
<td>4.0</td>
<td>3.5</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>range</td>
<td>0-13</td>
<td>1-12</td>
<td>0-11</td>
<td>0-10</td>
<td>0-10</td>
<td></td>
</tr>
<tr>
<td><strong>HADSDd</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>4.7 (2.8)</td>
<td>4.9 (2.8)</td>
<td>4.5 (2.5)</td>
<td>4.3 (2.0)</td>
<td>4.6 (1.8)</td>
<td>p = 0.210</td>
</tr>
<tr>
<td>median</td>
<td>5.0</td>
<td>4.0</td>
<td>4.5</td>
<td>4.0</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>range</td>
<td>0-11</td>
<td>0-11</td>
<td>1-10</td>
<td>2-10</td>
<td>2-8</td>
<td></td>
</tr>
</tbody>
</table>

1 = range 0–48, a lower score indicates more disabilities, 2 = range from 0 (no distress) to 21 (maximum distress)

**Correlations**

There was no correlation between the SEIQoL-DW index and physical function at any of the measurements; however, at TP 2, the SEIQoL-DW correlated negatively with depression (r_s = -.535, p = < 0.01) indicating that patients with lower score on the SEIQoL-DW had more symptoms of depression.

**Study II**

**Coping strategies**

Most commonly used coping strategies were support and independence early on after diagnosis (Figure 2). There was a change in the use of information seeking, which decreased from time point 1 to time point 2 (z = -2.851, p = < 0.01), and item 15 ‘I am philosophic about my illness, whatever will be will be’ increased to time point 2 (z = -2.161, p = 0.03). There was no difference in the use of different coping strategies with respect to gender. Patients ≤ 64 more often used positive action compared to those ≥ 65 at time point 1 (U = 60.00, p = 0.02), but no difference was evident at time point 2.
Figure 2. Mean scores for the different coping strategies and changes from TP1 to TP2. Maximum score for each coping strategy is 6.

Emotional distress and physical function

Fifteen patients were considered as doubtful/cases for anxiety at time point 1; at time point 2, this number had decreased to five. Four patients were considered as doubtful/cases for depression at time point 1, with a small increase to six patients at time point 2. There was no difference between gender for anxiety and depression at the two time points. There were no differences when comparing means for anxiety and depression at the two time points (data not shown). Patients’ physical function declined between the two time points (Table 7). There was no difference with respect to gender or age at the two time points (data not shown).

Table 7. Mean scores for ALS FRS-R and HADS subscales at the two time points.

<table>
<thead>
<tr>
<th></th>
<th>TP1 (n= 31)</th>
<th>TP2 (n= 28)</th>
<th>Change (n= 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALS FRS-R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>37.5 (6.5)</td>
<td>32.4 (10.3)</td>
<td>p = &lt; 0.01</td>
</tr>
<tr>
<td>range</td>
<td>23-46</td>
<td>10-46</td>
<td></td>
</tr>
<tr>
<td>HADSa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>6.5 (3.3)</td>
<td>5.3 (2.9)</td>
<td>p = 0.13</td>
</tr>
<tr>
<td>range</td>
<td>0-13</td>
<td>1-12</td>
<td></td>
</tr>
<tr>
<td>HADSd</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (SD)</td>
<td>4.7 (2.8)</td>
<td>4.9 (2.9)</td>
<td>p = 0.15</td>
</tr>
<tr>
<td>range</td>
<td>0-11</td>
<td>0-11</td>
<td></td>
</tr>
</tbody>
</table>
Correlation
There was a positive correlation between positive action and physical function at time point 1, indicating that patients with less physical disabilities used this strategy for coping more often. Patients using this strategy also reported less symptoms of depression. Independence was related to low emotional distress, and patients that used item 15 reported less symptoms of anxiety at time point 1. Patients with symptoms of depression had less positive thinking for coping at time point 2. Item 18 correlated positively with anxiety at both time points, indicating that patients with symptoms of anxiety kept their feelings to themselves instead (Table 8).

Table 8. Correlations between coping strategies, HADS and ALS FRS –R.

<table>
<thead>
<tr>
<th></th>
<th>HADSa TP1</th>
<th>HADSa TP2</th>
<th>HADSc TP1</th>
<th>HADSc TP2</th>
<th>ALS FRS-R TP1</th>
<th>ALS FRS-R TP2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive action</td>
<td>-0.046</td>
<td>0.001</td>
<td>-0.668**</td>
<td>-0.218</td>
<td>0.361*</td>
<td>0.357</td>
</tr>
<tr>
<td>Independence</td>
<td>-0.388*</td>
<td>-0.067</td>
<td>-0.507**</td>
<td>-0.218</td>
<td>0.300</td>
<td>0.095</td>
</tr>
<tr>
<td>Positive thinking</td>
<td>-0.127</td>
<td>0.006</td>
<td>-0.151</td>
<td>-0.498*</td>
<td>-0.245</td>
<td>-0.018</td>
</tr>
<tr>
<td>Item 15</td>
<td>-0.439*</td>
<td>-0.265</td>
<td>-0.350</td>
<td>-0.164</td>
<td>0.006</td>
<td>-0.027</td>
</tr>
<tr>
<td>Item 18</td>
<td>0.509*</td>
<td>0.498*</td>
<td>0.311</td>
<td>0.290</td>
<td>0.084</td>
<td>0.102</td>
</tr>
</tbody>
</table>

Spearmans ‘r rho * P = 0.05, ** P = 0.01

Study III
In this study, the patients were divided into groups, according to time in the study. Group 1 only participated at the first time point, and group 5 participated at all five time points. The dropout from one time point to another was due to patients being too ill to participate or had passed away.

Coping strategies
The results show that the patients used several different strategies for coping with the disease. The most frequently used strategies were support, independence and item 15 (I am philosophic about my illness; whatever will be will be) (Tables 9, 10 and 11). There seems to be no difference in the use of the different coping strategies between the groups. Thus, the use of different coping strategies does not seem to change much over time when comparing means (data shown in Paper III).
Table 9. Mean (SD) of Support

<table>
<thead>
<tr>
<th>Group</th>
<th>1 (n= 5)</th>
<th>2 (n= 7)</th>
<th>3 (n= 8)</th>
<th>4 (n= 4)</th>
<th>5 (n= 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>5.1 (0.7)</td>
<td>5.3 (0.6)</td>
<td>5.0 (0.5)</td>
<td>5.3 (0.6)</td>
<td>5.3 (0.7)</td>
</tr>
<tr>
<td>6m</td>
<td>5.0 (1.2)</td>
<td>4.8 (0.9)</td>
<td>5.2 (0.7)</td>
<td>4.7 (0.8)</td>
<td></td>
</tr>
<tr>
<td>12m</td>
<td>5.1 (0.6)</td>
<td>5.6 (0.4)</td>
<td>4.8 (1.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18m</td>
<td></td>
<td>5.3 (0.6)</td>
<td>5.2 (0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24m</td>
<td></td>
<td></td>
<td>5.0 (1.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Baseline = 1-3 months after diagnosis. Maximum score is 6.

Table 10. Mean (SD) of Independence

<table>
<thead>
<tr>
<th>Group</th>
<th>1 (n= 5)</th>
<th>2 (n= 7)</th>
<th>3 (n= 8)</th>
<th>4 (n= 4)</th>
<th>5 (n= 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.5 (0.7)</td>
<td>5.1 (0.7)</td>
<td>4.8 (0.7)</td>
<td>5.1 (0.4)</td>
<td>5.4 (0.6)</td>
</tr>
<tr>
<td>6m</td>
<td>4.7 (1.0)</td>
<td>4.8 (0.8)</td>
<td>5.2 (0.6)</td>
<td>5.1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>12m</td>
<td>4.6 (0.7)</td>
<td>4.6 (0.5)</td>
<td>5.0 (0.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18m</td>
<td></td>
<td>4.1 (0.7)</td>
<td>5.0 (0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24m</td>
<td></td>
<td></td>
<td>4.7 (0.9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Baseline = 1-3 months after diagnosis. Maximum score is 6.

Table 11. Mean (SD) of Item 15

<table>
<thead>
<tr>
<th>Group</th>
<th>1 (n= 5)</th>
<th>2 (n= 7)</th>
<th>3 (n= 8)</th>
<th>4 (n= 4)</th>
<th>5 (n= 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.2 (1.9)</td>
<td>4.6 (1.9)</td>
<td>4.9 (1.6)</td>
<td>4.7 (1.2)</td>
<td>4.6 (1.4)</td>
</tr>
<tr>
<td>6m</td>
<td>4.7 (1.7)</td>
<td>5.0 (1.7)</td>
<td>5.0 (0.8)</td>
<td>45.1 (1.4)</td>
<td></td>
</tr>
<tr>
<td>12m</td>
<td>5.6 (0.7)</td>
<td>4.8 (1.0)</td>
<td>4.5 (1.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18m</td>
<td></td>
<td>4.8 (1.0)</td>
<td>4.9 (1.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24m</td>
<td></td>
<td></td>
<td>5.2 (1.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Baseline = 1-3 months after diagnosis. Maximum score is 6.

The physical function

The mean score for the total group (n = 36) was 37.6 at baseline. The mean score for the ALS FRS-R shows that there was a difference in physical function between the groups at baseline, with lower score in groups 1 and 2 compared to groups 4 and 5 (Table 12). This result indicates that patients in groups 1 and 2 were more physically impaired compared to the other groups.
Table 12. Mean (SD) of the Total ALS FRS-R.

<table>
<thead>
<tr>
<th>Groups</th>
<th>1 (n= 5)</th>
<th>2 (n= 7)</th>
<th>3 (n= 8)</th>
<th>4 (n= 4)</th>
<th>5 (n= 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>33.0 (3.7)</td>
<td>31.3 (6.2)</td>
<td>39.4 (5.3)</td>
<td>40.7 (5.9)</td>
<td>41.5 (4.4)</td>
</tr>
<tr>
<td>6m</td>
<td>23.6 (9.6)</td>
<td>34.0 (6.6)</td>
<td>33.0 (15.8)</td>
<td>38.0 (5.6)</td>
<td></td>
</tr>
<tr>
<td>12m</td>
<td>24.9 (6.5)</td>
<td>22.8 (12.4)</td>
<td>35.2 (6.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18m</td>
<td>15.0 (9.7)</td>
<td>30.2 (10.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24m</td>
<td>26.2 (12.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Baseline = 1-3 months after diagnosis. Maximum score for the ALS FRS-R is 48.

Emotional distress

The results showed that although most patients did not suffer anxiety or depression during the disease progression, some patients had symptoms within the score for clinical anxiety and depression (Figure 3). The symptoms of clinical anxiety and depression were present during the first year after diagnosis, but were not found during the final two assessments.

Figure 3. Mean score for HADSa and HADSD. Maximum score for each subscale is 21.

Correlation

There were correlations between different coping strategies, between coping strategies and physical function, and coping strategies and emotional distress (Table 13). During the first year after diagnosis, depression correlated negatively with positive action, independence and positive thinking. There was a
positive correlation between anxiety and item 18 (I keep my feelings from friends and family), independence and item 18, and between support and positive thinking during the same period. From 18 months after diagnosis, physical function correlated negatively with item 15 (I am philosophic about my illness, whatever will be will be), but positively with item 18 and information seeking. There was also a negative correlation between depression and positive action at TP 5.

Table 13. Correlations between coping strategies, anxiety, depression and physical function at the different time points.

<table>
<thead>
<tr>
<th></th>
<th>P.F</th>
<th>P.A</th>
<th>I</th>
<th>A/V</th>
<th>I.S</th>
<th>P.T</th>
<th>Item 15</th>
<th>Item 18</th>
<th>Item 19</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.F</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.50d</td>
<td>0.53e</td>
<td></td>
</tr>
<tr>
<td>Anx</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.89e</td>
</tr>
<tr>
<td>Dep</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.64c</td>
<td>-0.67c</td>
<td>-0.53e</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.54e</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>-0.70f</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.54c</td>
<td>0.57LA</td>
<td>0.57e</td>
</tr>
<tr>
<td>P.A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.66c</td>
<td></td>
</tr>
<tr>
<td>Ind</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.55b</td>
<td></td>
</tr>
<tr>
<td>I.S</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.55e</td>
<td></td>
</tr>
<tr>
<td>P.T</td>
<td>0.61c</td>
<td>0.58LA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.84e</td>
</tr>
<tr>
<td>Item 18</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-0.56c</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Spearman’s rho, P < 0.01(2-tailed). P.F = physical function, Anx = anxiety, Dep = depression, S = support, P.A = positive action, Ind = independence, A/V = avoidance/venting, I.S = information seeking, P.T = positive thinking, Item.15 = philosophic, Item 18 = ‘hides feelings’, Item 19 = alternative therapies.  

Study IV
The care for the patient
The first content area was; relatives’ experiences of patient care. Relatives had a positive experience of the care and described that the care was based on the patient’s needs, with the goal of facilitating the situation for the patient. The theme for this content area was patient-centred care inspired a feeling of security and consisted of five categories: 1)the treatment provided by the staff, 2)help and support from the staff, 3)knowledge among the staff, 4)availability of the staff/care and finally 5)continuity of care.

The care was described as friendly and accommodating, and the staff were described as being perceptive, sensitive and listening to the patient’s
needs and desires. Most of the help and support related to assistance with different aids and solving problems, thus, facilitating the patient’s situation. If the patients did not get support from a specialised ALS team, relatives experienced that they had to find a solution to their problems on their own. Special knowledge among the staff was viewed as important and inspired a feeling of security. In contrast, lack of knowledge among health professionals near the patient’s home inspired a feeling of insecurity. Despite the limited availability of the ALS team, the care was experienced as being available when needed. Patients who lived far away from the ALS team experienced a lack of availability near the patient’s home. Continuity with regular appointments with the team and meeting the same staff member at each visit were viewed as important. Some relatives experienced that these visits tiring for the patient and felt that help and support could have been given over the phone instead.

Support for the relatives

The second content area was: Relatives’ experiences of support they received for themselves during the course of the disease. Most relatives had been offered support, and they were positive and grateful for the support. Despite this, the study showed that several relatives, due to various reasons, did not make use of the support that was offered. The theme for this content area was support was available, but different factors influenced use of it among the relatives. This second theme consisted of four categories: 1) support offered to relatives, 2) different support was needed/demanded, 3) the staff’s role in providing support, and 4) reasons why relatives did not benefit from support.

The support, provided by the staff in the ALS team to the relatives, was described as both practical and supportive. There was a difference in what kind of support the relatives needed. Some needed to talk about their situation, while others needed education, practical training and knowledge that could facilitate them to care for the patient. There was also a need for time to talk about the anger and grief, and an opportunity to ask questions without the patient being present. Straight and honest answers from the staff helped the relatives to manage the care and the situation. The ALS team should continue to provide the support, which must be repeatedly and continuously offered during the disease progression. The staff have an important role in providing support because of their knowledge and experience of the disease. There were different reasons as to why relatives chose not to use the support that was offered. The relatives felt that the support was based on the patient’s needs; they focused on the patient and were not able to think of their own situation or the staff could not answer their questions. Some relatives had to solve the problems on their own in order to cope with their situation.
Discussion

The purpose of the project was to follow patients from diagnosis and throughout a period of two years to evaluate quality of life, coping strategies and emotional well-being over time to get a wider knowledge of those topics that may occur during the disease progression. We also wanted to investigate relative’s experience of the care for the patient and the support they received themselves during the disease progression.

Decreased physical function over time is expected due to the illness characteristics, which is also shown in the present study with decreased mean values. In study III, the patients were divided into groups depending on length of time they participated in the study. Patients in groups 1 and 2 had lower mean scores on the ALS FRS-R compared to the other three groups, indicating that those patients were more physically impaired compared to those in groups 3–5. The mean score on the ALS FRS-R was higher in group 5 at all measurements.

Earlier studies have shown that symptoms of anxiety and depression are rare among ALS patients (108, 112). Even though there were few patients with symptoms of clinical anxiety and depression, several patients scored above the cut-off score for doubtful cases/cases early on after diagnosis compared to later in the study. Most of the patients with scores above the cut-off for clinical anxiety and depression were seen in groups 1–3, indicating that the patient with longer survival time suffered less of emotional distress compared to those who only participated during the first year after diagnosis. This may be due to faster disease progression among the patients in groups 1–3. Another explanation may be a prolonged diagnostic interval from onset to diagnosis, leading to emotional distress and more physical impairment at time of diagnosis. Even though we have not measured length of time from onset to diagnosis, and therefore cannot draw any conclusion, it must be taken into consideration as a possible explanation as to why patients in groups 1–3 had more symptoms of anxiety and depression compared to groups 4–5. The cases of clinical anxiety and depression were evident during the first year following diagnosis, but then declined, which indicated that it may be a psychological reaction to the ALS diagnosis (99).
Quality of life

Since the aim was to evaluate individual QoL among ALS patients, we used the SEIQoL-DW, which has been shown to be suitable for this purpose (129, 130). In accordance with other studies (73, 74), the results shows that family, friends and own physical health were important for the overall QoL. These areas dealt with social relations, fellowships, to support and be supported by family and friends, physical functions, symptoms depending on the disease and treatment. The percentage for each area indicated that the patients might change areas of importance during the disease progression. For example, the area Sport/exercise decreased and the area Support increased over time. The disease leads to impaired physical function, which could be an explanation for the results. By adjusting to the situation and focusing on what the patient can still do, they take control over the situation, which may help them to maintain good QoL (131). Studies have shown that perceived control is associated with positive feelings of well-being (132, 133). Several studies have shown that physical function is not necessarily important for the QoL in ALS (60, 74, 78, 81, 134, 135). Despite this, patients often rate their own health as being of importance for their QoL. Further knowledge is needed on this subject to understand the relationship between health and QoL.

The patients rated their QoL as relatively good, and despite increased physical disability, the QoL index remained stable over time, which also has been found in earlier studies (74, 76, 77, 136, 137). It is often assumed that ALS patients have poor QoL and that the disease leads to deterioration in QoL. The results from present study, supported by other studies on the subject, show the opposite and highlight the impossibility to validate other individuals’ QoL and the importance of measuring this topic on an individual basis. HRQoL can be described as the gap between the patients’ expectations of health and their experience of it (68). The experience depends on how well the results agree with expectations. Patients with a progressive disease, leading to changing clinical status, may change their expectations during the disease and therefore report the same level of QoL over time despite the decreased physical function. The iQoL index did not correlate with physical function, and one explanation could be that patients re-evaluated the areas of importance depending on increased physical impairment due to the disease. This re-evaluation may be explained by the response shift theory; according to this theory, the patients reappraised values, internal standards and conceptualisation of QoL over the disease trajectory (138, 139). This may also explain the stability of QoL index over time.

The results show that SEIQoL-DW correlated with depression; this correlation was seen early on after diagnosis. This supports the findings of the study by O’Doherty et al. (78) evaluating QoL in neurological illnesses, but is in contrast to Tramonti et al. (2012) who found no correlations between iQoL and depression (140). It is difficult to draw any conclusion on these
findings, but in our study and the study by O’Doherty et al. (2010), newly diagnosed patients were included. There is no information on disease duration among the participants in the study by Tramonti et al. (2012) but difference in length of time from diagnosis may explain the differences in the result.

Coping

There are a few studies with the aim to explore the variation in different ways of coping among newly diagnosed ALS patients. Present study focuses on evaluating strategies used to cope with the disease. It seems that anxiety and depression have negative impact on the patients’ ability to cope with the diagnosis (141). Moreover, results of this present study indicate that the use of coping strategies correlate with the patients well-being; however, we cannot say if it is the coping strategies that affect the well-being or vice versa.

The results from studies II and III showed that ALS patients use variety of strategies to cope with the disease. Early on after diagnosis (i.e. 1–3 months after diagnosis), the patients used support and independence to cope with the disease. The use of information seeking decreased, and item 15 ‘I am philosophic about my illness, whatever will be will be’ increased during the first six months after diagnosis. The specific type of coping strategies that had been used did not differ much over time. Most of the patients in our study used support and independence as a way to cope, more than they used avoidance/venting strategies for coping. This result is in agreement with the study by Matuz et al. (89). However, our patients used support more frequently, compared to the patients in the study by Matuz et al. (2010), which can be due to the welfare system in Sweden, where most aid and support are available for free or available at low cost to the patient. Previous studies have shown that patients with ALS often use problem-focused coping strategies to deal with the disease (87, 142, 143). Our results indicate that patients use problem-focused strategies and adapt to their illness. In our study, we found that information-seeking decreased between the two time points, in contrast to a study by Hetch et al. (2002) where information-seeking increased time (143). This difference may depend on the difference in time from diagnosis to first interview between these two studies, with duration of 1–3 months in our study and 16 months in the study by Hetch et al. (2002). The results also showed that the use of item 15 ‘I am philosophic about my illness, whatever will be will be’ increased over time, indicating that the patients adapt to their illness, which may also explain the decreased use of information-seeking among our patients. Rabkin et al. (2009) found that ALS patients often approached the disease philosophically, and the rates of depression seem to be lower than expected (144). These findings are in agreement with our results. The question that arises is whether the coping strategies affect the emotional
well-being or if it is vice versa, or perhaps there are no relationships between
the use of coping strategy and emotional well-being. There was a significant
correlation between physical function, emotional well-being and age with
the use of different coping strategies in study II. Similar to the findings by
Cupp et al. (2011) (115), we did not find any correlation between physical
function and emotional well-being. Lee et al. (2001) also found a correlation
between the use of different coping strategies and physical function or psy-
chological well-being (125), which is in agreement with our findings. Non-
correlation was found between men and women and different coping strate-
gies. The results show that ALS patients use both problem-focused and emo-
tion-focused strategies to cope with the disease, which is in agreement with
other findings (136). Lazarus and Folkman (84) describe coping as a process
where the individual uses both cognitive and behavioural efforts to handle
the demands that arise due to the situation. They also assume that coping
efforts change during the disease progression. The present study confirmed
the use of both cognitive and behavioural strategies to cope with the disease.
Our results show that there were only few changes in use of coping strategies
during the disease progression. Nonetheless, it must be taken into considera-
tion that we analysed data on group level. Perhaps, if we had analysed it on
individual level it may be a different result. It is difficult to compare our
results with others because of the variation in the use of coping instrument
and the difference in patients included in the studies.

Relatives’ experience

Most of the care and support was about practical help with providing aids
and solving problems. This help did not just facilitate the patients’ situation,
but it also helped relatives to manage the care for their loved one. The results
confirmed the importance of multi-disciplinary care, with knowledge and
understanding of the disease and care when helping and supporting ALS
patients and their relatives (56, 59). This specialised knowledge helps the
staff to provide the specific aids needed and solve problems, and the
knowledge helps the relatives to gain a feeling of security in their situation.
The results also showed that health professionals in the patient’s home dis-
trict need education and support in caring for ALS patients. Some relatives
described a need to have access to a team close to their home, which was
lacking. Furthermore, relatives also needed education and training in provid-
ing care (38, 145) and being prepared for what is to come (146).

Most relatives did not think of their own situation; instead, focus was on
the patient’s needs, which is in accordance with previous studies on pallia-
tive care (58, 145, 146). By focusing on the patient and keeping themselves
busy, they took control over the situation (50, 147, 148). Relatives need sup-
port, which focuses on their needs (149); despite this, few relatives talked
about emotional support in the interviews, instead they focused on practical help. Relatives who participate in the care of a dying patient need to be seen as an indirect patient. The relatives need support to feel that they have enough knowledge and can feel secure in being able to participate in the care of a loved one (150).

This thesis highlights the need for individual measurement of iQoL, coping and need for support among patients and relatives during the disease progression. This individual measure can be used to identify and prioritise problems of importance for the individual patient, which probably will help the health professionals to provide care and support from the patients' own perspective. Further research is needed, probably with both quantitative and qualitative measurements, to get a deeper understanding of factors that influence iQoL, the use of coping strategies, and the relationship between iQoL, coping and emotional well-being.

**Methodological considerations**

Since ALS is a rare disease, we decided to do a multi-centre study, including ALS teams from different parts of Sweden. An invitation was sent out to several hospitals, but only two (except for our own) agreed to participate. The first author performed all data collection in the form of home visits. The teams helped to include patients and relatives based on the inclusion criteria. The strengths of studies I, II and III are the prospective design, with newly diagnosed ALS patients who met the inclusion criteria and who accepted participation. There were few dropouts between the different time points, despite the severity of the disease, probably due to the fact that all data collection was performed in accordance with home visits. The fact that all data collection was performed in the form of home visits by the first author may explain the low number of drop-outs. With this method, we could also guarantee that no data were missing and that the participants filled out all questions. It was also possible to ask for clarification if any questions arose when completing the questionnaires. The limitation in this study is the small sample size and the fact that patients who had difficulties in completing the questionnaires were assisted by the data collection researcher, which must be kept in mind when interpreting the results. Another limitation is that some patients were excluded due to their psychological status or they declined participation in the study because they felt distressed, which may have influenced the results. Depending on the characteristics of the disease, only a few instruments were chosen for data collection with the goal that the patients should manage to participate even though the disease becomes worse. This could hopefully reduce the drop-out rate and may be one explanation as to the few drop-outs in present study. We would probably have gotten a deeper
understanding on coping and quality of life if both quantitative and qualitative instruments had been used for data collection. That would probably give more information on factors that affect these topics and provide information from patient’s own perspective on how to better support them during the disease progression.

The SEIQoL-DW has been shown to be reliable and valid in measuring QoL among patients with ALS (130, 151). By describing the areas nominated by the patients, and not just name them, we achieved a better understanding, which can be used in clinical practice. The use of the instrument may be limited among patients with impaired cognitive function, since it requires insight into factors which determine one’s QoL, and an ability to think abstractly (67). Some of the participants with severe symptoms had practical difficulties to complete the SEIQoL-DW. Patients with weakness in arm or hand had difficulties to use the VAS to determine the level of function and the pie chart for weighting each cue. For those patients, the data collection researcher made the rating, following directions from the patients. This may have influenced their rating, which must be taken into consideration. If the participants’ cannot nominate five cues, a prompt list could be used. Here, this list was not used; instead, the patients were permitted to nominate less than five cues because we did not want to affect the choices made by the patient. If the patient just mentioned four areas, it is probably only those four areas that are of importance, and it would not give any deeper understanding on the topics.

The MND coping scale (125) only measures the use of different coping strategies to cope with the disease; it provides no information on whether the strategies help the patients to cope well or poorly with the disease, or factors that may influence the use. Lazarus (1993) described the need for measuring the specific threats separately rather than the overall illness (85). The MNDCS focuses on the strategies used for coping with ALS. To gain a deeper understanding of how patients cope with ALS, we need to use a combination of different instruments, with both quantitative and qualitative approaches. The questionnaire was relevant and easy to use when tested before start of the study. The instrument consists of 22 items, 18 of which are divided into six domains. Lee et al. (2001) who designed the instrument recommend the user to use all 22 items. Some of the studies that have used the MNDCS describe the questionnaire as a 22 item scale, but only present the results for the six domains (i.e. 18 item scale). This affected the possibility to compare our results with others. Item 15, which is not included in any of the six domains, was one of the most often used strategies in our study; therefore, it would have been interesting to see if this was in agreement with other studies or if it was specific to our participants.

All instruments used in this thesis have been used in several scientific studies and have been considered valid and reliable. There are no standards for what an acceptable Cronbach’s alpha coefficient should be, but a value of
0.70 or higher is considered as sufficient (120). The MND coping scale had low Cronbach alpha in all sub-scales. This may be due to the small sample size in our study and few items in each sub-scale. Another explanation could be that our sample had a very narrow range of coping. The Cronbach’s alpha coefficient increases with spread of variance of scores (152). The Cronbach’s alpha for avoidance/venting was negative, indicating a very weak and negative correlation between the items in that sub-scale. A negative Cronbach’s alpha could indicate that some questions are reversed and that those responses should be recoded, but when checking we found nothing wrong. Other studies, where the MNDCS was used, had not given an account of Cronbach’s alpha. It is therefore difficult to say if the low value is specific for the present study, or if it is due to the instrument. The internal consistency of ALS FRS-R and HADS was satisfactory.

The trustworthiness in qualitative research is mostly discussed in terms such as: credibility, dependability, and transferability (128). The strength of study IV is the variation amongst the participants; our study comprised both spouses and children, and the participants had different ages and genders from two different departments of neurology with the purpose of capturing different kinds of experiences. This variety in the sample, strengthened the credibility. The credibility is also strengthened by the choice of interviews for data collection, which made it possible to gain insight into relatives’ experience of the care for the patient and the support they received for themselves. Data collection by interviews has many advantages, for instance, the right person answers the question and data are collected in the same way regardless of the multi-centred approach (127). The analysis has been performed by two authors and finally discussed among all co-authors. A limitation in the trustworthiness could be that the first author, who performed the interviews, had also been involved in providing care for some of the patients. This involvement could be both positive and negative. Relatives who know the interviewer may be more open and feeling more motivated to answer the question with hope of improving the care and support. In contrast, relatives from other teams may be reluctant to talk negatively about or criticize their staff in the presence of another ALS-team. The hope is that it did not influence the interviews among any of the participants. The second author listened to eight randomly selected interviews to determine whether there were any differences with regard to previous acquaintanceship. No differences were detected in how questions were posed and followed up. The first author’s pre-understanding of the disease and the relatives’ situation during the disease were considered to be useful when conducting the interviews and analysing the data. It can also be viewed the other way around, meaning that this pre-understanding had influenced the interpreting of the data. To retain dependability, a semi-structured interview guide was used with follow-up questions when necessary. One aspect to consider is whether the order in which the questions were asked might have affected the results. By starting
to ask questions about their experience of the care for the patient, before discussing their experiences of the support they received themselves, the focus may have shifted onto the patient rather than the relatives, which may have affected the results. Study IV should perhaps have been divided into two studies, with interviews at different time points to better catch the relatives’ needs. The fact that the interviews were conducted 6-12 months after the patients had died may be a weakness, with the risk that the relative’s memory of the care and support may have been affected. This may have influenced the results, but it was of great ethical importance to give the relatives time to mourn before contacting them. In contrast, it could also be viewed as a strength since the relatives have had time to get a better perspective and reflect on their past situation, which hopefully meant that they could freely discuss the issues without feeling obligated. The transferability in present study was strengthened by describing the characteristics of the participants, the different steps of the analysis and presenting citations, which supported the results.
Conclusion

The studies in this thesis included areas such as quality of life, coping strategies and emotional well-being in newly diagnosed ALS patients over a two year period. It also included experiences from relatives about the care for the patient and the support they received themselves.

- The results showed that patients rated their quality of life as good and their overall quality of life did not change over time, despite decreased physical function.
- Areas such as family, friends and own physical health were the most nominated areas of importance for their QoL; however, when looking at the weight for each area, it was shown that both family and own physical health were more important compared to friends.
- Support and independence were the most used coping strategies early on after diagnosis. Support involved maintaining relationships with family and friends and different aids, which helped the patient to be independent and to cope with the disease.
- The use of coping strategies change over time early on after diagnosis, and the patients’ psychological well-being was correlated to different coping strategies.
- The care and support must be based on individual needs for both patients and relatives. It is important that the health professionals responsible for the care have knowledge and experience of the disease and care.
- The relatives’ focus was on the patients’ situation; therefore, it is important that health professionals are observant of the relatives and offer them help and support so that they can better manage their situation.
- The results show that the family is of great importance for both QoL and coping for ALS patients. The results also showed that relatives need different kinds of support during the disease progression. This highlights the importance of including and supporting family members, so that they feel secure and are able to support the patients during the disease progression.
Svensk sammanfattning (Swedish summary)

Bakgrund
I Sverige insjuknar ca 250 personer per år i amyotrofisk lateral skleros (ALS). Sjukdomen karakteriseras av ett successivt bortfall av de motoriska nervceller som kontrollerar den viljestyrda muskulaturen, och patienten utvecklar successivt muskelsvaghet. Orsaken till sjukdomen är okänd och det finns idag ingen botande behandling för ALS. Cirka 50 % av patienterna avlider inom 3 år från symtomdebut, ofta till följd av andningssvikt. Vården inriktas på att möte de fysiska, psykiska, emotionella och existentiella behov som uppstår under sjukdomen. Att drabbas av ALS innebär en förändring för hela familjen och många anhöriga deltar aktivt i vården av den sjuke.

Tidigare studier som undersökt livskvalitet, coping och emotionella besvär hos ALS patienter över tid har vanligtvis inkluderat patienter med olika sjukdoms duration, och det finns enligt vår vetenskap ingen longitudinell studie där man studerat dessa områden hos enbart nydiagnostiserade ALS patienter.

Syfte
Det övergripande syftet med denna avhandling var att prospektivt studera livskvalitet, coping och emotionella besvär hos nydiagnostiserade patienter med ALS och följa dem under två års tid. Ett ytterligare syfte var att undersöka anhörigas upplevelse av vården för den sjuke samt stödet som de själva erhöll under sjukdomstiden. Genom ökad kunskap kring dessa frågor ökar våra möjligheter att på bästa sätt hjälpa dessa patienter och deras anhöriga.

Metod
Detta var en deskriptiv studie med både kvalitativa och kvantitativa metoder. Samtliga nydiagnostiserade patienter med ALS som vårdades av ALS teamen vid Akademiska sjukhuset i Uppsala, Mälarsjukhuset i Eskilstuna samt Västmanlands sjukhus i Västerås, och som uppfyllde inklusionskriterierna, tillfrågades om deltagande. Totalt deltog 36 patienter i studie I och III, och 33 patienter i studie II. Patienterna följdes med frågeformulär samt intervju
1-3 månad efter diagnos och sedan var 6:e månad under en period av två år med avseende på livskvalitet (SEI-QoL-DW), coping strategier (MND-coping scale) och depression och ångest (HADS). Patienternas fysiska för- måga skattades med hjälp av en funktionsskattningsskala (ALS FRS-R). För att undersöka anhörigas upplevelse av vården för den sjuke samt stödet till dem själva genomfördes semistrukturerade intervjuer 6-12 månader efter att patienten avlidit. I denna studie deltog totalt 15 anhöriga från Akademiska sjukhuset i Uppsala samt Mälarsjukhuset i Eskilstuna.

Resultat

Familjen, vänner samt egna hälsan var de viktigaste områdena för patienternas individuella livskvalitet. De flesta patienter skattade sin livskvalitet som god, och det var få förändringar över tid trots att deras fysiska förmåga för- sämrades. Det fanns ett samband mellan livskvalitet och depression tidigt efter diagnos, dvs patienter som skattade sin livskvalitet som dålig hade symptom på depression. Däremot var det ingen korrelation mellan livskvalitet och fysisk hälsa vid någon tidpunkt.

Patienterna använde framför allt strategier som stöd (support) samt att vara självständig/oberoende (independence) för att hantera sjukdomen. Däremot använde de sällan strategier som undvikande/ventilering (avoidance/venting) eller att söka information (information seeking). Användandet av strategier förändrades något tidigt efter diagnos, men var sedan relativt stabilt över tid. Det var ingen skillnad mellan män och kvinnor vad gäller användandet av olika strategier, men däremot var det en skillnad beroende på ålder. Patienter som var 64 år eller yngre använde oftare positivt handelande (positive action) jämfört med dem som var 65 år eller äldre vid första mätningen, men det var däremot ingen skillnad vid andra mätningen. Det fanns ett samband mellan emotionellt välstående och olika coping strategier, dessa korrelationer sågs framför allt under det första året efter diagnos. Även patientens fysiska för- måga korrelerade med olika coping strategier, dessa korrelationer sågs i ett senare skede av sjukdomen.

Diskussion/slutsats

Resultatet visar att sociala relationer samt stöd och hjälp har stor betydelse för både den upplevda livskvaliteten och hanteringen av sjukdomen (coping) vid ALS. Trots att de flest patienter skattade sin livskvalitet som god, och att flertalet patienter inte hade tecken på ångest och depression så belyser studien vikten av individuellt stöd för både patienter och anhöriga under sjukdomsförloppet. Det var få förändringar i användandet av copingstrategier över tid, men det är ändå viktigt att vara medveten om de få förändringar som kan vara.

De flesta patienter skattade sin livskvalitet som relativt god, och den var stabil över tid trots sjukdomens karaktär. En förklaring till detta kan vara att patienten omvärderar och omprioriterar vad som är viktigt för dennes livskvalitet till följd av sjukdomen. Trots att tidigare studier ofta nämner att livskvaliteten vid ALS inte påverkas av den fysiska funktionen så visade resultatet att den egna fysiska hälsan var av stor betydelse för patientens livskvalitet. Studien klargör inte på vilket sätt hälsan påverkar livskvaliteten men det är viktigt att medvetande göra att detta område har en inverkan på livskvaliteten.

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76. Olsson AG, Markhede I, Strang S, Persson LI. Differences in quality of life modalities give rise to needs of individual support in patients with ALS and their next of kin. Palliative & supportive care. 2010;8(1):75-82.


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