Optimizing quality of care for patients with ALS and their family caregivers
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General Discussion
The overall aim of this thesis is to optimize multidisciplinary ALS care through expanding our knowledge on previously identified bottlenecks in complex ALS care – prognostication, the provision of aids and adaptations, and caregiver strain – and to investigate the added value of case management in a mixed methods research project.

In the absence of a cure for ALS or effective interventions to slow down or stop the progression of muscle weakness, the quality of ALS care requires continuous attention. Existing guidelines lack conclusive evidence on aspects of ALS care, indicated by patients and/or caregivers as shortcomings e.g., symptom treatment, caregiver strain, care coordination, communication between health professionals, provision of aids and adaptations. This thesis focused on patients with ALS as well as their caregivers and included the following topics: 1) prognostication of the rate of functional decline as a consequence of the disease, 2) the procurement of assistive devices and home adaptations (ADHA), 3) client-centered supportive care for patients and their caregivers, and 4) caregiver strain.

In this chapter the main findings of the previous chapters are discussed and issues concerning the methodology are critically reviewed. The implications of the findings for clinical practice are considered and, finally, recommendations for further research are made.

**MAIN FINDINGS**

The systematic review revealed that the current evidence on prognostic factors for functional decline in ALS is insufficient to allow the development of a prediction tool that can support clinical decisions (chapter 2). Due to the limited data and inconsistency of results in the small number of studies included, the quality of evidence for the prognostic value of age at onset, site of onset, time from symptom onset to diagnosis, and ALSFRS-Revised baseline score was low. The prognostic value of initial rate of disease progression, age at diagnosis, forced vital capacity, frontotemporal dementia, body mass index, and comorbidity remains unclear.

Recent literature confirmed part of the prognostic factors we derived and identified additional prognostic factors. The studies of Hothorn (2014), Atassi (2014) and Küffner (2015) were based on the same data from the PRO-ACT database. In our literature search, we found only one study for uric acid as a non-significant prognostic variable for disease progression. However, the Atassi study (2015; n=4,838) showed that higher uric acid levels at baseline were predictive for a slower drop in ALSFRS-R (p=0.01). Therefore, we upgraded the overall quality of evidence (in accordance with our GRADE approach) for uric acid from ‘no’ into ‘very low’ evidence. The weighing of the other prognostic variables within these recent studies in addition to our findings did not result in an upgrade of the overall quality of evidence, mainly due to the quality factors inconsistency and imprecision.
The relevance of the prognostic factors we found was strengthened by previous reported prognostic factors for survival in the critical review of Chio et al. (2009) and in later conducted prognosis studies \(^6\text{-}^{11}\). Partly conflicting findings were reported by Wolf et al. (2015) who found male gender related to worse prognosis \(^{11}\).

Küffner and colleagues (2015) presented the results of a crowdsourcing competition for prediction models of disease progression \(^5\). The best predicting model of disease progression adequately distinguished between patients with a slow and fast disease progression. Compared to this prediction model, clinicians misclassified 35 percent of the patients, so it seems that the model might offer added value to the physician in patient counseling. The authors announced that the utility of the best models of the competition will be tested in a clinical setting \(^5\). However, the studied models resulted in a prediction of the slope of functional decline, and lack the prediction of functional milestones during the disease, like loss of ambulation, ADL independency, and verbal communication. Clinical practice shows that besides information on disease duration and rate of decline, patients also want to be informed about the nature and sequence of the progressive functional limitations.

Previous studies have attempted to build prediction models for survival \(^{12}\text{-}^{13}\). Although these models can be valuable for research purposes, they lack reliability for use as a credible algorithm in individual patient care. Significant uncertainty remains around estimating individual survival time. Recently Elamin et al. (2015) \(^{10}\) validated a prognostic index for survival and Wolf et al. (Neuroepidemiology, 2015) \(^{11}\) presented a model to predict the survival probability at the time of diagnosis for an individual patient. Within these studies, prognostic factors easily available at the first clinic visit, were used. Most patients also want to be informed about the nature and sequence of the progressive functional limitations, and physicians want reliable, predictive information about the functional course for accurate symptom management. The model of Elamin (2015) \(^{10}\) included executive dysfunction which showed to be a significant prognostic factor for shorter survival and Wolf’s model (2015) \(^{11}\) included early cognitive decline independently related to shorter survival. The information generated from survival studies might be useful for the development of prognostic models for the rate of functional decline, as corresponding factors for functional decline and survival enhance prediction reliability. In literature, there is a debate about the usefulness of the generally used disease stratification by site of onset or type of motor neuron dominance. Turner et al. (2013) suggested stratification by 1) rate of disease progression, defined as the time to spread to a new region, and 2) degree of cognitive impairment \(^{14}\). Possibly these stratifications might well be better alternatives in ALS clinical practice as they seem to better fit the functional limitations patients are confronted with. The model of Elamin (2015) is promising and provides clues for further development of a reliable prognostic model for the functional decline of the individual patient \(^{10}\).

One of the practical issues of disease management in ALS in which prognostication plays a fundamental role are assistive devices and home adaptations (ADHA). Confronted with
the problems during the process of procuring ADHA within the context of the Dutch healthcare system and based on earlier literature findings, we performed a nationwide survey in 2007 to gain insight in the experiences and problems from the viewpoint of patients with ALS. The results of our cross-sectional study described in chapter 3 underscored our clinical experiences and the earlier findings with respect to problems during the ADHA procurement process despite multidisciplinary support. Seventy-one percent of the surveyed patients were supported by specialized multidisciplinary ALS care teams. Fifty-eight percent of the patients reported problems in obtaining ADHA. Patients with ALS viewed time delay and the authorities’ lack of disease knowledge as the most prominent requiring improvement in the procurement process.

Quick and easy (=minimal bureaucracy) procurement procedures, increased awareness of all stakeholders involved, reliable prognostication and empowerment of the patients and their caregivers in the application process might enhance patient and caregiver satisfaction with the service delivery systems and outcomes.

To fill the aforementioned gaps in ALS care, we hypothesized that case management might be effective to improve quality of care (QOC). Our cluster RCT on case management in multidisciplinary ALS care demonstrated no significant benefit of case management to the patients’ QOL, caregivers’ strain and patients’ and caregivers’ QOC when added to standard multidisciplinary care compared with standard care alone (chapter 4). Most striking was that patients as well as caregivers rated the overall quality of ALS care for the patient as good. Caregivers rated the care for themselves to a slightly lesser extent as good. An explanation for the earlier reported gaps in Dutch ALS care might be that a non-recurring negative experience does not have a profound influence on how patients and caregivers rate the overall QOC we asked them to weigh. The ‘low’ scores on the ALSAQ-40 domain Emotional Functioning, the primary outcome, indicating a relatively low impact of the disease on the patient’s well-being, are remarkable. These ‘low’ scores on QOL, indicating a better emotional functioning, and the relatively high scores on QOC imply that there was little room for improvement through intensive case management, and might be an explanation for the lack of effect of the intervention within the Dutch ALS care setting.

Patients and caregivers differed in their need for case management. One quarter of the patients and their caregivers made no appeal to the case manager. But on the other hand, 31 caregivers and 48 patients raised at least one issue during the 12 months intervention period. The actions undertaken by the case manager during the intervention, were aimed at improving quality of care (e.g., symptom treatment, care coordination, ADHA realization), providing emotional support and reducing caregiver strain. This was confirmed by the findings of our qualitative study on the perspectives and service needs of patients with ALS, their spousal caregivers and healthcare professionals on case management in addition to the usual multidisciplinary ALS care (chapter 5). Both patients and caregivers being interviewed appreciated the practical and emotional support of the case manager. Professionals
(rehabilitation medicine consultants and case managers) did not mention the added value of emotional support by the case manager. Patients, caregivers and healthcare professionals indicated that case management can have surplus value in specific situations. Factors that emerged from the interviews and the focus group and appeared to influence patients’ and caregivers’ needs for and receptiveness to case management are less functioning of the ALS care team, a rapid disease progression, personal factors (e.g., maladaptive coping styles, less self-assertive, less self-sufficiency and reluctant to ask for support) and inadequate support from the social network of patients and caregivers. Participants valued the house calls, ample time to talk with patients and caregivers and proactive approach of the case manager. These aspects of the case management intervention might be usable as additional support for vulnerable patients and caregivers. We conclude that there is insufficient evidence to implement our case management model in the Dutch ALS care setting. The interviews with participants and the focus group discussion resulted in a greater understanding of the ALS care needs from the different perspectives.

As highlighted in chapter 4, the case management intervention did not reduce caregiver strain. More than that, in both study groups caregiver strain increased significantly during the intervention period. This stressed the need for more insight in factors related to (increase of) caregiver strain and a more prominent role of ALS care interventions targeting caregiver strain. The data from longitudinal assessments within our RCT showed that apart from the amount of functional limitations and condition of emotional well-being of the patient, a passive (avoidant) coping style of the caregiver, increased feelings of anxiety, and feeling less supported by the ALS team impact on the strain of ALS caregivers (chapter 6). In order to regulate caregiver strain and to tailor multidisciplinary ALS care to the caregivers’ needs, ALS care teams should increase their support for the caregiver and implement caregiver intervention programs that focus on caregiver’s coping style and distress. Evidence in scientific literature for interventions targeting caregiver strain in ALS lacks 17,18. Care support for informal caregivers should be based on individual needs and on two-sided aspects: the caregiver in the care for the patient and in the care for themselves 19,20.

**METHODOLOGICAL CONSIDERATIONS**

*Study population*

The large sample sizes within our longitudinal studies strengthened the reliability of our results. Together with the comparability of our study participants with those of a Dutch population-based epidemiology study, we are confident that the conclusions we made hold for the Dutch ALS population 21. Inherent to longitudinal studies of patients with ALS is the high missing rate due to death during the study or because participating the study becomes too burdensome.
The numbers of dropout participants and intermittent missing data within both study groups of the case management RCT resulted in an equal proportion of evaluations within both groups. We found a difference, although not significant, between both groups in the number of patients who died (intervention n=23, control n=15) and who stopped (intervention n=5, control n=10) during the study period. Patients who died had older age, lower FVC predicted and lower ALSFRS-R total score at baseline compared to patients who stopped. We are confident that this did not result in a bias of treatment effect estimate on QOL or QOC since the baseline scores of the patients who died or stopped on the outcome measures QOL and QOC did not differ. The baseline CSI scores of their caregivers was significantly higher in patients who died compared to those who stopped (mean (SD): 7.0 (2.7) versus 4.7 (3.1); p=0.03), possibly resulting in a distortion of the intervention effect on caregiver strain. However, controlling for this baseline difference in our multilevel analysis would have contributed to an even larger negative value of the multilevel regression coefficient for the effect of the case management intervention on caregiver strain we found (β= -0.08; p=0.15). A strength of the multilevel analyses of the longitudinal data we conducted is that these analyses use all available data in the estimation of the model parameters.

Due to the randomization of the multidisciplinary ALS care teams instead of the participants, potential RCT participants knew in advance which study group they would be assigned to participate. Considering participating the study or not might be influenced by that. However, forty-six percent participation willingness of the patients from the intervention teams and forty-three percent of the control teams clarifies that there was no difference in the willingness of potential patients and their caregivers to participate in the RCT.

Study design
The mixed methods approach – RCT and qualitative study case management – allowed us to better understand the intervention outcomes and the meaning and relevance of the intervention for the participants. Köpke and McCleery (2015) in their editorial on systematic reviews of case management for patients with dementia and their caregivers stated that the inclusion of non-RCT evidence like qualitative studies might contribute to disentangle the complex care intervention case management, which was confirmed by our mixed methods approach.

By investigating determinants of caregiver strain using data captured in the randomized controlled trial on case management, relevant determinants of strain may have been missed. We did not ask our participants which patient and caregiver factors, according to their opinion, contribute to caregiver strain. An additional qualitative study probably might have resulted in more insight in patient and caregiver factors associated with caregiver strain as experienced by participants. However, semi-structured interviews with purposive selected participants (patients, caregivers, physicians) of the RCT case management
showed that informal caregiver care needs are related to suboptimal care provided by the multidisciplinary ALS team, a rapid disease progression, personal factors of patients and caregivers and a poor social network. Assuming an association between caregiver strain and content of care these results indicate the surplus value of additional qualitative research.

The intervention case management
Within the RCT the contrast between usual care and usual care plus intensive case management was not strong enough to demonstrate an intervention effect. Patients and caregivers experienced usual care of a very high quality so that additional case management had no added value. Our qualitative analysis showed that the range of tasks of the case manager fitted the needs of the participants and any shortcoming in ALS care. We assume that within the Dutch ALS care setting a differing case management model likewise would show comparable results.

Participants of our qualitative study indicated that the timing of the case management intervention was not optimal. Either case management was offered too late – participants already put things into action by themselves – or participants regretted that the intervention had to stop after 12 months. This finding confirms the importance of timing of disease management with respect to offering support for patients with ALS and their caregivers. The use of an inception cohort and an extended intervention duration in our opinion would not have resulted in a different study result due to the above mentioned interpretation.

Outcome measures
The primary outcome in the RCT on case management was the patients’ health-related QOL assessed with the 40-item ALS Assessment Questionnaire (ALSAQ-40), domain Emotional Functioning (EF). The EF domain addresses various emotional problems, for example, feeling lonely, feeling hopeless about the future, and feeling embarrassment in social situations. Possibly not all aspects of emotional well-being are covered with the 10 items of EF. Other, in ALS research sparingly used generic global QOL measures (e.g., SEIQOL, SEIQOL-DW, SMILE, McGillQOL) are more focused on domains of QOL such as the existential domain (meaning in life, perception of purpose, spirituality, religion) or on those life areas which are important to the individual patient’s QOL (e.g., family, household, work, speech). Given the content of our intervention, the choice of one of these QOL outcome measures in our opinion would not have led to a differing RCT outcome as we did not find an effect on any other outcome measure.

At baseline, we expected differences in processes, structures and outcomes of care provided by the single ALS care teams and the judgement of this care by the participants. As a result of the randomization, the quality of care was equally rated in both RCT study groups. We used a 10-point scale to assess perceived QOC by asking participants to indicate with a report mark (1=very poor QOC, 10=excellent QOC) their opinion about the ALS care in
its entirety during the past month. We did not assess specific domains or items of QOC and did not make distinction in structures, processes and outcomes of care. Consequently, we did not know how participants weighted different aspects of ALS care, such as professional expertise, accessibility, client-centeredness, availability of ADHA, symptom management and the frequencies of the team contacts. ALS specific QOC measurements are not yet available and in literature suggestions are made to develop an ALS QOC instrument which includes the domains of satisfaction with care for patients with ALS. Stephens et al. (2015) concluded no differences in QOC outcomes between patients attending and not attending multidisciplinary clinics, and indicated that other QOC instruments are needed to demonstrate the benefits of multidisciplinary care. Today in Dutch clinical practice other methods are used to assess the experienced quality of ALS care, such as self-administered or generic QOC questionnaires, mirror meetings and after-death evaluations with informal caregivers. In our opinion, the development of an ALS specific QOC instrument for patient and caregiver care could be a valuable addition to ALS care and research.

We used versions of the ALSFRS(-R) as outcome measure for functional decline. Franchignoni et al. (2013 and 2015) demonstrated that the ALSFRS-R lacks unidimensionality. In contrast to the heterogeneity of the ALSFRS(-R) total score, the domains of the ALSFRS(-R) (bulbar, motor, and respiratory functions) appear unidimensional, and adequately represent the respective constructs. Grimby and colleagues (2012) reported that treating an ordinal summed rating scale as an interval measure assuming equal intervals, and subjecting such scale to parametric statistics, will likely lead to invalid results. This might be an explanation for the low level of evidence for the prognostic factors we found in our review. Grimby et al. (2012) consider it of importance to use Rasch analysis and Rasch derived instruments to allow a valid interpreting of data derived from ordinal rating scales. In line with Grimby’s study (2012), we suggest to use modern test theory in the development and evaluation of ALS specific instruments.

In addition, results from earlier studies on the ALSFRS(-R) total score showed that this score does not meet the assumption of a linear decline for statistical models in prognostic studies. We suggest that a thorough revision of the ALSFRS-R through the item response theory paradigm (IRT) or the development of an ALS specific composite measure with biomarkers for disease progression (e.g., uric acid, creatinine, blood pressure) might contribute to a more reliable clinical reproduction of functional decline during the entire disease course. Until the availability of such a measure, we recommend to utilize the ALSFRS-R domain scores in daily practice and clinical research.

To measure caregiver strain in ALS, we chose the generic Caregiver Strain Index (CSI) as it is widely used in clinical practice and health care research. Mockford et al. (2009) developed and validated the on carer report based MND Carer Questionnaire (MNDCQ), measuring the extent to which dimensions of caring affect caregivers’ health. The authors indicated that an increase of the MNDCQ score suggests a higher level of caregiver strain.
burden and that the instrument may be used to identify the individual caregiver needs. In continuation of the Mockford study, which is based on the UK’s health care system, we suggest to develop a combined qualitative and quantitative ALS specific caregiver strain assessment tool including both positive and negative aspects of caregiving as well as an ALS specific caregiver needs instrument 41,42.

**Generalizability**
Outcomes of case management interventions are reported within other diseases, but comparing these study results is difficult due to differences in outcome measures and case management models used. Relevant characteristics of our studied samples (age, gender, site of onset and time to diagnosis) within the ADHA study, the RCT case management study and the caregiver strain study did not differ from those of the 1128 incident patients in the population based register in the Netherlands 21. As patients characteristics within the study of Huisman et al. (2011) were comparable with other national population based studies, we conclude that our results can be generalized across populations 21. However, we have to remark that patients with cognitive or behavioural impairments were excluded from participating our RCT study, which potentially limits the generalizability of our RCT and caregiver strain study. In addition, the possible differences in (the quality of and accessibility of) health care systems, treatments availability, settings, religions and ethnicities across the different countries, causes that we cannot extrapolate our findings to the entire ALS population.

**CLINICAL IMPLICATIONS**

**Case management**
The findings of our RCT on case management do not support the implementation of this case management model as part of ALS care in the Netherlands. However, aspects of case management might be a valuable contribution to multidisciplinary ALS care: house calls, ample time for consultation, emotional support and proactive care. Tailored care is the key to ALS care that best fits the personal care needs of patients with ALS and their informal caregivers. Health care professionals should prompt patients and caregivers, if susceptible, to think about (near) future topics and care needs. Through reflections and sharing emotions patients and caregivers might feel supported in coping with their situation. Structural monitoring of and discussing ALS care with patients and their caregivers contributes to timely discovery of bottlenecks in care. To offer a central contact person (e.g., one of the members of the ALS team), easily accessible, might be the link between multidisciplinary care and the individual care needs of the patient and caregiver. Attentiveness of the multidisciplinary care team for factors that might play a part in the patient’s or caregiver’s need for additional
support is advisable: an insufficient social network and lack of social support, shortcomings in the usual care, a rapid disease progression rate, the disease stage, and personal factors of patients and caregivers (e.g., passive coping styles, limited resilience, less assertive, less self-sufficient, reluctant to ask for support). Possibly a quick scan of these factors during the RMC consultations could help.

ALS care teams should be continuously alert on the quality of care the teams provide to the patients and their informal caregivers. Periodic quality of care evaluations should be a standard within ALS care and monitoring as well as discussing the quality of ALS care with patients and their caregivers offer opportunities to adjust care to their needs.

Prognostication
The available knowledge concerning the prognostic factors we found in our systematic review and on reported prognostic factors for survival might help physicians when considering the patient’s disease course (slow, moderate or rapid disease progression) \(^6\)\(^\text{-}\)\(^1\)\(^1\). Based on our results we recommend initial quantitative assessment of the following prognostic factors at the patient’s baseline visit at the RMC: age at onset, site of onset, time from symptom onset to diagnosis, baseline ALSFRS(-R) score, initial rate of disease progression, FVC, FTD, BMI, and comorbidity. This assessment might help the clinician to make a prognostic estimate at baseline. In informing patients about their prognosis, the clinician should acknowledge their likely inaccuracies, and discuss possible scenarios for the disease course. By monitoring disease progression (ALSFRS-R, FVC, BMI) during follow-up visits, prognosis can be adjusted if necessary.

To identify clinical ALS phenotypes with consistent prognostic patterns, population based data are needed \(^1\)\(^4\). It is of great importance to assess the clinical development of ALS – the display of clinical phenotyping and disease heterogeneity within patients – in order to achieve reliable prognostication of patients with ALS \(^5\). Comprehensive longitudinal data collection, with international standardized measurements of patient, disease, and intervention variables recorded in daily clinical practice and entered into large electronic databases, might enhance the possibility of identifying reliable prognostic factors \(^4\)\(^3\). These data preferably are based on inception cohorts. It’s the challenge for ALS care teams to inform patients with ALS about the importance of this type of research so patients are motivated to participate.

Given current advances in knowledge about the role of genetics in ALS, it is likely that the genetic variation in ALS will be unravelled to clinically more homogeneous subtypes in the future. This new knowledge might contribute to the development of prediction tools \(^4\)\(^4\).
ADHA
Based on our results we suggest different approaches for improvement of the procurement process:

- A proactive approach by all stakeholders – authorities, agencies and suppliers – to attain timely realization of the needed ADHA through increasing awareness of ALS and the impact on patients’ functioning. An online training for service providers related to this issue may contribute to achieve care improvement. (http://www.mndcare.net.au/overview/online-training-for-service-providers/mnd-aware) In 2011, the Netherlands ALS Foundation started an ALS awareness campaign to inform the Dutch public about this incurable disease and the impact on the patient’s daily life. (http://www.als.nl/stichting-als/reclamecampagnes/ik-ben-inmiddels-overleden/) The international ice-bucket challenge hype in 2014 resulted in an unprecedented media attention for ALS and contributed to an immense increase of familiarity with ALS within the public worldwide (http://www.alsa.org/about-us/ice-bucket-challenge-faq.html?referrer=http://www.google.nl/)45.

- The patient as information carrier to transfer (written) knowledge to all relevant parties about the disease, the consequences for independence and autonomy, the functional prognosis and the ALS care network might be the key to increased ALS awareness of all those involved. The ALS care teams, ALS patient associations, ALS knowledge centers and ALS funding agencies possibly may want to contribute to the preparation of an up-to-date package. As an example, the Dutch neuromuscular patient organisation (Spierziekten Nederland) developed information brochures for primary care physicians, for home care services and personal care assessors. (https://www.spierziekten.nl/overzicht/amyotrofische-laterale-sclerose/voor-hulpverleners-over-als/)

- Empowerment of patients and their caregivers by the multidisciplinary ALS care team through tailored psycho-education about ALS, ADHA, and the procurement procedures, so patients and caregivers learn to enter into dialogue with authorities, agencies and providers 46,47. Lack of clarity of the legal procedures and lack of information on what patients can expect from authorities, agencies and providers might be tackled through revision of the quality of current patient information 48,49.

- An emergency procedure for a demand-oriented indication and realisation process of ADHA for patients with ALS, endorsed by all stakeholders. Experiences within regional projects in the Netherlands so far showed that bureaucracy can be reduced and fast delivery is feasible. These projects might serve as best practice models for improving national quality of ALS care related to ADHA. Due to the variability in how the national health care systems organize their ADHA provision, the implementation of improvements will have to be tailor-made to these systems.

- Supporting the timing of proactive application of ADHA by monitoring the disease course and adequate prognostication. A task for the multidisciplinary ALS care team to
inform those patients who are ready to discuss this topic in order to timely start up the procurement process. However, as stated before, the current knowledge on prognostic factors to inform the individual patient about the course and time-span of the disease, hampers health care professionals in prescient recommendations. Improvements in predicting the rate and nature of functional impairments will contribute to decrease the time-span wherein AHDA applications are realized.

Monitoring and registration of the time points and outcomes of the entire procurement process of ADHA of each patient should be standard within ALS care to gain insight in the time phases of the process and to provide authorities and agencies with reliable feedback if problems arise. Empowerment of the patient and the caregiver by the ALS care team in their role during the procurement process might contribute to increased satisfaction with the process.

Caregiver strain
The vital role of informal caregivers in supporting patients with ALS is well recognized but caregivers are often vulnerable and overlooked by health care professionals. Health care professionals should increase their attention for the caregiver to fit their support to the needs of the caregiver. There are several methods to structure this attention: frequently asking the caregivers about their experiences with the changing situation and their workload, recurrent use of a valid disease-specific caregiver strain inventory, to survey the above-mentioned patient and caregiver factors, to formulate the aims of support for the caregiver within the ALS care plan and through regularly checks for additional support needs. For the latter, a caregiver needs questionnaire could be used. The timing of offering information and support facilities, and the realization of needed support is essential during the entire disease process. Finally, health care professionals should inform the informal caregiver about the availability of support after bereavement by the ALS care team or community care professionals.

RECOMMENDATIONS FOR RESEARCH / FUTURE PROSPECTS
It would seem that QOL and QOC of patients with ALS differ among countries. When we compare the QOL scores (ALSAQ-40 domain EF) within the RCT case management with scores in other countries, there is a striking difference in favour of the Dutch ALS population. Studies of patients’ and caregivers’ perceptions on QOC are scarce. By comparing data on QOL and QOC of patients and caregivers and on outcomes of QOC within different ALS health care systems, we might get more insight in the effectiveness of the different systems and the differences in QOL and QOC, which will contribute to the improvement of ALS care. Furthermore, more insight is needed in the association between QOL (e.g.,
mood, physical limitations, communication, fatigue) and QOC to know which QOC indicators (e.g., falls, respiratory status, nutritional status, survival, pain, salivation, caregiver burden, accessibility, client-centeredness, professional expertise) should be manipulated in order to maintain a satisfactory level of QOL for patients with ALS and their caregivers. In addition, it is suggested to conduct more qualitative studies to investigate aspects of quality of ALS care, as expectations and experiences of patients, caregivers and health care professionals might contribute to gain insight in structures, processes and outcomes of ALS care. International collaboration between ALS knowledge centres will facilitate this type of research. An ALS specific instrument for measuring patient and caregiver satisfaction with care, needs to be developed in consultation with patients and caregivers.

In continuation of our cross-sectional study, a longitudinal study, quantitative as well as qualitative, is needed to further investigate the experiences of incident patients and caregivers in the entire procurement process and the outcomes of ADHA. Within the Dutch ALS care setting it would be of interest to repeat our study to evaluate the effectiveness of the ALS awareness campaign and the implementation of ALS information packages for home care workers and personal care assessors (https://www.spierziekten.nl/overzicht/amotrofische-laterale-sclerose/voor-hulpverleners-over-als/). Registering data on ADHA in daily practice, available for patient management and research purposes and without extra burdening for patients and their caregivers, might help to improve ALS care.

It is proposed to conduct prospective comprehensive internationally data collection within inception cohorts, with standardized measurements of patient, disease and intervention variables to identify prognostic factors that have predictive value for a decline in ALSFRS-R domain scores and related functional milestones. Aim is to come to more reliable evidence synthesis of prognostic factors for functional decline in individual patients. The psychometric properties of the ALSFRS-R should be thoroughly revised and validated through Rasch analysis. It needs to be sorted out if an ALS specific composite measure with biomarkers for disease progression (e.g., uric acid, creatinine, blood pressure) might contribute to a more reliable clinical reproduction of functional decline during the entire disease course. The in January 2014 started ALS-Care research project (http://www.neurodegenerationresearch.eu/fileadmin/Project_Fact_Sheets/PDFs/Healthcare_Evaluation/ALS-Care_Fact_Sheet_Template.pdf) offers opportunities to come to significant improvements in measuring functional decline and prognostication of functional milestones.

Our findings contributed to more insight in caregiver strain in ALS. The currently available caregiver strain questionnaires should be reviewed and an ALS specific questionnaire including positive and negative aspects of caregiving should be validated for the ALS caregiver population. The effect of the patients’ cognitive and behaviour deficits on the strain of their informal caregivers needs further study and interventions to support informal caregivers confronted with those deficits, should be developed and implemented.
Behavioural and/or psychological interventions (e.g., meaning centered psychotherapy) targeting the patient’s emotional well-being should be developed. The development of a psycho-educational intervention to offer caregivers the opportunity to get insight in their mental imbalance related to strain and anxiety, and the implementation of stress managing strategies to enable caregivers to deal with their tasks and responsibilities should also be subject to further research. Longitudinal studies to assess ALS caregivers’ needs, to develop ALS caregiver behavioural (e.g., cognitive behaviour therapy) and/or psychological interventions (e.g., psycho-education) and to determine the effectiveness of caregiver interventions in ALS are needed. Recently, the Netherlands ALS Center started a research project on informal caregivers of patients with ALS. (http://www.als-centrum.nl/kennisbank/project-mantelzorgers/) Aim of this project is to find an adequate, evidence based approach to support these caregivers in their roles and thereby contributing to the patients’ well-being. The effect on the caregivers’ and patients’ QOL will also be examined.

GENERAL CONCLUSION

The overall aim of this thesis was to optimize multidisciplinary ALS care through expanding our knowledge related to previously identified bottlenecks in complex ALS care. The systematic review revealed that the current evidence on prognostic factors for functional decline in patients with ALS is insufficient to allow the development of a prediction tool that can support clinical decisions. The nationwide survey to explore the experiences of patients with ALS during the procurement of ADHA indicated that patients viewed time delay and the authorities’ lack of disease knowledge as the most prominent requiring improvement in the procurement process. The RCT on case management showed that patients with ALS and their informal caregivers in general rate the quality of the Dutch ALS care as good. The intervention case management in addition to usual ALS care showed no benefit with respect to the patients’ QOL, caregivers’ strain and the QOC for the patients and their caregivers. Based on the interviews and focus group within the qualitative study of the case management project we concluded that ALS teams can consider implementation of valued aspects of case management (accessibility, home visits and ample time, proactive approach, emotional support) in usual multidisciplinary care. Additional support might be provided to patients with rapidly progressive disease course, passive coping style and small social network. Finally, the longitudinal study on factors associated with caregiver strain over time identified that apart from the patient’s physical disability and emotional well-being, a passive coping style of the caregiver, increased symptoms of anxiety and feeling less supported by the ALS-team impact on the strain of ALS caregivers. The multidisciplinary teams involved with the care of patients with ALS need to be aware of these factors and increase their attention for the caregiver. We conclude improvements in knowledge and insight into the
bottlenecks determined at an earlier stage, but also into clues for advances in ALS care and further research. Our recommendations for improvements in multidisciplinary ALS care to fit the individual care needs of patients and their caregivers are:

- Provide tailor made, proactive care to the patient and the informal caregiver.
- Discuss the quality of ALS care with the patient and informal caregiver.
- In the interest of both the patient as the caregiver; take care for the caregiver.
- Stay alert for vulnerable patients and caregivers: a rapidly progressive disease course, an inadequate coping style, a less supportive or an inadequate social network and being less self-assertive or less self-sufficient.
- ALS health care professionals should be easy accessible.
- Consider to appoint a central contact person within the multidisciplinary ALS care team.
- Empower the patient and caregiver in the procurement process of ADHA.

An ALS specific instrument for measuring patient and caregiver satisfaction with care should be developed in consultation with patients and caregivers.

It is proposed that increased knowledge on prognostication might contribute to a more efficient procurement process of ADHA, improvements in care planning and timing of symptom management. More international collaborative research on prognostic factors for the functional decline in ALS is suggested. It is recommended to develop an ALS specific composite measure including biomarkers for disease progression (e.g., uric acid, creatinine, blood pressure) for reliable measurement of functional decline during the entire disease course.

Decrease of time-delay and increase of disease knowledge are indicated priorities to improve the procurement process of ADHA. Points for improvement are suggested to achieve a better rating for the entire procurement process. In addition, a survey of methods used within the ALS care teams to optimize the procurement process might lead to best practices, as there are differences in structures, processes, care networks, and care provision between the ALS teams.

The informal caregiver’s well-being is in the interest of both the patient as the caregiver. Therefore, appropriate tailor made support for the caregiver should be one of the aims of the multidisciplinary ALS teams. Our study findings provide clues for caregiver and patient support and, with the involvement of caregivers and patients, for further development of evidence-based supportive interventions. An ALS caregiver needs assessment tool for clinical purpose might be the next step towards improved care for caregivers.

The establishment of a national ALS Care and Research Network within the Netherlands ALS Centre will be an organizational foundation for the further development of excellent quality of care and care research in ALS and for intensive international collaboration within the studied care topics.
REFERENCES


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