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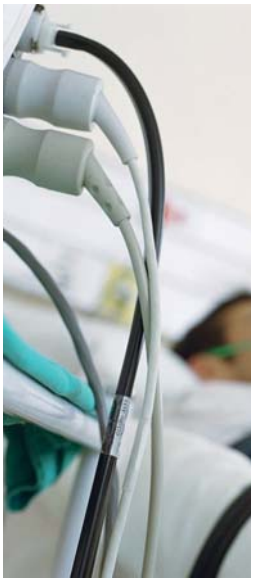

Forskning på amyotrofisk lateralsklerose Litteratursøk

Systematisk litteratursøk med sortering

folkehelseinstituttet

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Innhold

Hovedfunn

Nasjonalt kunnskapssenter for helsetjenesten fikk i oppdrag fra Helsedirektoratet å utføre et systematisk litteratursøk etter systematiske oversikter og pågående primærstudier om behandling og oppfølging av mennesker med amyotrofisk lateralsklerose (ALS).

Metode
Vi utførte et systematisk litteratursøk i flere databaser. Søket ble utført i november 2015 og potensielt relevante referanser ble sortert etter tema.

Resultater
Vi identifiserte 132 mulige systematiske oversikter og 141 pågående primærstudier:

- Flertallet av de identifiserte systematiske oversiktene omhandlet effekt av ulike legemidler. Det var også mange systematiske oversikter om ventilasjonsstøtte, fysioterapi eller trening.
- Tolv systematiske oversikter oppsummerte kvalitativ forskning på pasienter og pårørendes opplevelser og erfaringer.
- Tre systematiske oversikter omhandlet sammenhengen mellom ulike faktorer og pasientenes livskvalitet.
- De fleste pågående primærstudiene omhandlet effekten av ulike legemidler. Det var også mange studier om stamcellebehandling og ventilasjonsstøtte. Fem av de pågående studiene var fra et nordisk land.

Vi har ikke vurdert studienes metodiske kvalitet eller lest artiklene i fulltekst. Vi kan derfor ikke trekke noen konklusjoner om studienes resultater eller være sikker på at de oppfyller alle kriterier for systematiske oversikter. Vi søkte ikke etter avsluttede publiserte primærstudier. Vi presenterer sammendragene fra de systematiske oversiktene og lenker til de pågående studiene.

Tittel:
Forskning på amyotrofisk lateralsklerose. Litteratursøk.

Publikasjonstype:
Systematisk litteratursøk med sortering
Systematisk litteratursøk med sortering er resultatet av å
- søke etter relevant litteratur ifølge en søkestrategi og
- eventuelt sortere denne litteraturen i grupper presentert med referanser og vanligvis sammendrag

Svarer ikke på alt:
- Ingen kritisk vurdering av studienes kvalitet
- Ingen analyse eller sammenfatning av studiene
- Ingen anbefalinger

Hvem står bak denne publikasjonen?
Kunnskapssenteret har gjennomført oppdraget etter forespørsel fra Helsedirektoratet

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Når ble litteratursøket utført?
Søk etter studier ble avsluttet november 2015

Key messages

The Norwegian Knowledge Centre for the Health Services was commissioned by the Norwegian Directorate of Health to conduct a systematic literature search of systematic reviews and ongoing primary studies on the treatment and follow-up of patients with amyotrophic lateral sclerosis (ALS).

Methods

We conducted a systematic literature search in several databases. The search was completed in November 2015, and relevant references were sorted according to subject.

Results

We identified 132 potential systematic reviews and 141 ongoing primary studies:

- Most of the systematic reviews were about the effect of different drug treatments. There were also many potential systematic reviews on ventilation support, physical therapy and exercise.
- 12 systematic reviews summarized qualitative research on the perceptions and experiences of patients and their carers.
- 3 systematic reviews were about the correlation betweeen different factors and the patients' quality of life.
- Most of the ongoing primary studies were about the effect of different drug treatments. There were also a number of studies on stem cell treatment and ventilation support. Five of the studies were from a Nordic country.

We have not critically evaluated the studies and not read them in full text. Therefore, we cannot draw any conclusions regarding the studies' results, and some of the identified overviews may not be truly systematic reviews. We did not search for completed and published primary studies.

We present abstracts from the identified systematic reviews and URLs to the ongoing primary studies.

Title:
Research on amyotrophic lateral sclerosis. Literature search

Type of publication:
Systematic reference list
A systematic reference list is the result of a search for relevant literature according to a specific search strategy. The references resulting from the search are then grouped and presented with their abstracts.

Doesn't answer everything:
- No critical evaluation of study quality
- No analysis or synthesis of the studies
- No recommendations

Publisher:
Norwegian Knowledge Centre for the Health Services

Updated:
Last search for studies:
November 2015.

Forord

Nasjonalt kunnskapssenter for helsetjenesten, nå Kunnskapssenteret i Folkehelseinstituttet, fikk i november 2014 i oppdrag fra Helsedirektoratet å lage en oversikt over oppsummert forskning og pågående primærforskning om amyotrofisk lateralsklerose (ALS).

Når forskningsfunn benyttes som beslutningsgrunnlag, bør det tas utgangspunkt i tilgjengelig forskning med best mulig kvalitet. Studiedesign, utførelse og analyser påvirker vår tillit til studienes resultat. I dette arbeidet har vi ikke lest artiklene i fulltekst eller vurdert den metodiske kvaliteten av dem. I vedlegget til Kunnskapssenterets håndbok "Slik oppsummerer vi forskning" finnes det sjekklister som kan brukes til å vurdere kvaliteten av ulike typer studier. Sjekklistene kan være gode hjelpemidler i det videre arbeidet med å ta stilling til forskningens kvalitet, herunder gyldighet og troverdighet. Håndboken med sjekklister er tilgjengelig på nettsiden til Kunnskapssenteret http://www.kunnskapssenteret.no/verktoy/slik-oppsummerer-vi-forskning.

Signe Agnes Flottorp	Liv Merete Reinar	Ingvild Kirkehei
Avdelingsdirektør	*seksjonsleder*	*prosjektleder*

Innledning

Problemstilling

Vi søkte etter systematiske oversikter og pågående primærstudier på behandling og oppfølging av mennesker med amyotrofisk lateralsklerose (ALS).

Bakgrunn

Amyotrofisk lateralsklerose (ALS) er en sjelden muskelsvinnsykdom hvor nervecellene som sender signaler fra hjernen til musklene blir gradvis svekket. Dette rammer hjernen, hjernestammen og ryggmargen, og musklene som mister sin nerveforsyning bli gradvis svakere og tynnere. De første symptomene merkes ofte som svekkelse i en arm, et bein eller utydelig tale (1).

ALS er en progredierende sykdom og forekommer oftest hos personer over 50 år. Menn rammes litt hyppigere enn kvinner. I Norge er det ca. 300-400 som har diagnosen ALS. Det oppstår ca. 1-2 nye tilfeller pr. 100.000 innbygger hvert år. Gjennomsnittlig levetid etter at diagnosen er stilt, er 3 år, men med betydelige variasjoner (2).

Det finnes ingen kjent behandling i dag som kan helbrede sykdommen. Medikamentet Riluzol bremser sykdommens utvikling og forlenger overlevingstiden, men fører ofte til bivirkninger som diare og muskelstivhet (1, 2). Andre behandlinger kan dempe symptomene og lindre plager som spastisitet, muskelskjelettsmerter, pustevansker, slim i luftveiene og angst (2). Det gis blant annet tiltak innenfor fysioterapi, ergoterapi, logopedi, ernæring, spyttsekresjon og ventilasjonsstøtte (1).

Primærstudier og systematiske oversikter

I denne rapporten har vi identifisert og sortert mulige systematiske oversikter og pågående primærstudier om ALS.

Primærstudier er «undersøkelser, som innsamler og bearbeider original- (dvs. primær-) data fra klienter, pasienter osv. Eksempler på forskjellige typer primærstudier er randomiserte forsøk, observasjonsstudier, case studier mm.» (oversatt definisjon) (3).

Mange primærstudier registreres ved studiestart i såkalte studieregistre. De fleste studiene som registreres er kliniske studier som undersøker effekten av ulike tiltak. Noen registre inneholder observasjonsstudier, og det finnes også registreringer av kvalitative studier (4). Det finnes et rekke nasjonale og internasjonale studieregistre og norske studier registreres i ClinicalTrials.gov. På nettsiden WHO International Clinical Trials Registry Platform kan man søke i et stort antall studieregistre.

En systematisk oversikt oppsummerer resultater fra en eller flere primærstudier. Kunnskapssenteret definerer en systematisk oversikt slik: «En oversikt over et klart definert forskningsspørsmål. Oversikten bruker systematiske og eksplisitte metoder for å identifisere, utvelge og kritisk vurdere relevant forskning, samt for å innsamle og analyse data fra studiene som er inkludert i oversikten. Statistiske metoder (meta-analyser) vil i noen tilfeller bli brukt for å analysere og oppsummere resultatene fra de inkluderte studiene. I andre tilfeller skjer oppsummering uten bruk at statistiske metoder.» (5)

Styrker og svakheter ved litteratursøk med sortering

Ved litteratursøk med sortering gjennomfører vi systematiske litteratursøk for en gitt problemstilling. Resultatene fra søket blir grundig gjennomgått for å sortere ut ikke-relevante artikler. Dette gjøres basert på tittel og sammendrag. Artiklene innhentes ikke i fulltekst. Det gjør at vi kan ha inkludert studier som ville vist seg ikke å være relevante ved gjennomlesning av fulltekst. Vi benytter kun databasesøk for identifisering av litteratur og kan derfor ha gått glipp av potensielt relevante studier. Andre måter å identifisere studier på, som søk i referanselister, kontakt med eksperter på fagfeltet og upublisert litteratur, er ikke utført i dette oppdraget. Ved litteratursøk med sortering gjennomfører vi ingen metodisk kvalitetsvurdering av artiklene og vi sammenstiller ikke resultatene.

Ved en full forskningsoppsummering ville vi ha innhentet artiklene i fulltekst for endelig vurdering opp mot inklusjonskriteriene. Inkluderte studier ville så blitt kvalitetsvurdert i henhold til våre sjekklister og resultatene ville så blitt sammenstilt og diskutert.

Metode

Vi utførte et systematiske søk etter systematiske oversikter og pågående primærstudier. Søkeresultatet ble gjennomgått i henhold til på forhånd definerte inklusjonskriterier.

Inklusjonskriterier

Vi inkluderte systematiske oversikter og pågående primærstudier publisert f.o.m. år 2000 som omhandlet ALS og et av følgende tema:

1. Effekt av behandlingstiltak, f.eks. akupunktur, fysioterapi, trening, ergoterapi, legemidler, musikkterapi, respirator eller stamcellebehandling.
2. Effekt av tiltak rettet mot pårørende
3. Livskvalitet
4. Pasienter og pårørendes opplevelser og erfaringer (kvalitativ forskning)
5. Kostander og kostnadseffektivitet ved ulike behandlingstiltak
6. Nordiske studier på biomarkører, genetikk, komorbiditet, diagnostikk av ALS, årsaker og risikofaktorer
7. Europeiske eller Nord-Amerikanske studier på forekomsten av ALS

Litteratursøking

Prosjektleder og forskningsbibliotekar Ingvild Kirkehei (IK) utførte systematiske søk i følgende databaser: MEDLINE, Embase, PsycINFO, CINAHL, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessments Database (HTA), Epistemonikos, PubMed, PEDro og OT Seeker. Publikasjonslister fra SBU, Sundhedsstyrelsen, FINOHTA, Nice og CADTH ble gjennomgått. Prospero ble søkt for å finne pågående systematiske oversikter. Siste søkt ble utført i november 2015.

I august 2015 ble det søkt etter pågående primærstudier i studieregistrene Clinical Trials.gov og Who International Clinical Trials Registry.

Vi utførte et bredt søk, sammensatt av emneord og tekstord for amyotrofisk lateralsklerose og relaterte diagnoser som motor neuron disease og Lou gehrig's disease. Søket i MEDLINE, PubMed, Embase, Cinahl og PsycINFO ble avgrenset med søkeord for

systematiske oversikter. Søket ble ikke avgrenset til språk, tiltak eller utfall. Fullstendig søkestrategi finnes i vedlegg 1.

Artikkelutvelging og sortering

En person leste gjennom søkeresultatet, valgte ut relevante referanser og sorterte dem på temaene nevnt i tidligere avsnitt om inklusjonskriterier. Temaene ble valgt etter ønske fra oppdragsgiver. Publikasjonenes sammendrag ble kopiert fra kildene hvor publikasjonene var blitt identifisert.

Utvelging av litteratur ble gjort kun basert på tittel og sammendrag. Vi leste ikke artiklene i fulltekst og har ikke vurdert studienes metodiske kvalitet eller sammenstilt resultatene. Det betyr også at vi kan ha inkludert referanser som ved lesing av fulltekst viser seg å være usystematiske oversiktsartikler eller som ikke tilfredsstiller kravene til en systematisk oversikt. På bakgrunn av dette beskriver vi de identifiserte referansene som «mulige» systematiske oversikter. Det betyr også at referansene kan være feilsortert og ikke relevante i forhold til temaet. Sorteringen er ikke gjensidig ekskluderende og det kan være overlapp mellom temaene.

Resultater

Søket etter systematiske oversikter resulterte i 1750 referanser. 289 av disse var mulige systematiske oversikter om ALS, hvorav 132 oppfylte inklusjonskriteriene. 14 var systematiske oversikter under utvikling.

Vi inkluderte systematiske oversikter som handlet om ALS alene, eller oversikter hvor ALS ble nevnt som en av flere sykdommer.

Søket etter pågående primærstudier resulterte i 216 registreringer, hvorav 141 oppfylte inklusjonskriteriene.

Antall identifiserte systematiske oversikter og pågående studier fordelt på temaer vises i tabell 1.

Tab. 1: Systematiske oversikter og pågående studier fordelt på temaer

Tema	**132 mulige systematiske oversikter**	**141 pågående studier per nov. 2015**
Effekt av tiltak		
- Ulike behandlinger	21	
- Akupunktur	2	
- Ernæring	6	
- Fysioterapi, trening og ergoterapi	15	9
- Kommunikasjonsteknikk	1	
- Kramper og spastisitet	2	
- Legemidler	30	74
- Lysbehandling		1
- Menneske-maskin interaksjon	2	7
- Musikkterapi	1	
- Organisering	1	1
- Pårørendetiltak		2
- Psykologiske tiltak	1	
- Spyttsekresjon	6	
- Stamcellebehandling /genterapi	3	28
- Søvnproblemer	1	
- Tale	1	

- Transkraniell magnetisk stimulering	1	3
- Tverrfaglig behandling	1	
- Strålebehandling		1
- Ventilasjonsstøtte	14	14
Opplevelser og erfaringer	11	
Livskvalitet	3	
Økonomi	2	
Forekomst	6	1
Etikk	1	

Flertallet av både de identifiserte systematiske oversiktene og primærstudiene omhandlet effekt av ulike legemidler. Det var også mange systematiske oversikter om ventilasjonsstøtte, fysioterapi eller trening. 21 av de systematiske oversiktene omhandlet to eller flere ulike behandlingstiltak og ble derfor sortert i en egen kategori. 11 systematiske oversikter oppsummerte kvalitativ forskning. Vi fant en mulig systematisk oversikt over studier på etikk.

32 systematiske oversiktene var publisert i 2014 eller 2015. 11 var publisert mellom 2000 og 2005. 89 var publisert mellom 2006 og 2013.

Omkring halvparten av de pågående primærstudiene undersøkte effekten av ulike legemidler. Det var også mange pågående studier om stamcellebehandling og ventilasjonsstøtte.

Blant de pågående studiene var det en fra Danmark, tre fra Sverige og en fra Finland. Ingen studier var fra Norge.

Andre kilder til forskning på ALS

Referansene som er identifisert i denne rapporten gir ikke et fullstendig bilde av forskningsaktiviteten innenfor feltet ALS.

Avsluttede publiserte primærstudier

Vi har i dette prosjektet ikke søkt etter avsluttede publiserte primærstudier, kun de som er registrert som «pågående». For å få et fullstendig bilde av forskningen på et område, vil det være nødvendig å søke etter primærstudier, spesielt der hvor man kun har systematiske oversikter av eldre dato. Det kan også finnes mange publiserte primærstudier som ikke er fanget opp av de identifiserte systematiske oversiktene.
Viktige kilder for søk etter primærforskning er databasene MEDLINE/Pubmed, Embase og Cochrane CENTRAL.

Pågående studier

Ikke alle pågående studier registreres i de to studieregistrene vi har søkt i. ALS Therapy Development Institute i USA har en oversikt over pågående studier på ALS fra hele verden; «ALS Clinical Trials» http://www.alstdi.org/als-research/als-clinical-trials/. Oversikten oppdateres jevnlig.
ALS Norsk støttegruppe informerer om utførte og pågående studier her:
http://alsnorge.no/informasjon/forskning/

Kliniske oppslagsverk

I tillegg til systematiske oversikter og primærstudier, kan det være nyttig å lese om amyotrofisk lateralsklerose i kliniske oppslagsverk som BMJ Best Practice og UptoDate. Begge kilder er tilgjengelige på www.helsebiblioteket.no.

Et søk på «ALS» i UptoDate finner f.eks. «Symptom-based management of amyotrophic lateral sclerosis» (6) og "Disease modifying treatment of amyotrophic lateral sclerosis" (7). Man kan også lese om diagnostikk, "clinical features" og forekomst av ALS.

Retningslinjer

Databaser for retningslinjer kan også være viktige kilder til oppsummert forskning. National Guideline Clearinghouse og G-I-N er eksempler på kilder.
Et søk på «amyotrophic» i National Guideline Clearingshouse gir 14 treff:
http://www.guideline.gov/search/search.aspx?term=amyotrophic%20lateral&sub-term=amyotrophic.

Systematiske oversikter

Nedenfor vises tabeller over identifiserte og sorterte referanser til mulige systematiske oversikter. De nyeste oversiktene vises først.
Tabell 1 viser systematiske oversikter som har undersøkt effekten av to eller flere tiltak. De etterfølgende tabellene er sortert alfabetisk på tema.
Pågående systematiske oversikter vises i en egen tabell på s. 101. Se rapportens innholdsoversikt for ytterligere informasjon om temaer og sidetall.

Effekt av tiltak

Flere ulike behandlingstiltak

Tab. 1: Systematiske oversikter som har undersøkt effekten av to eller flere ulike behandlingstiltak.

	Referanse	Sammendrag
1.	Bucchia M, Ramirez A, Parente V, Simone C, Nizzardo M, Magri F, et al. **Therapeutic development in amyotrophic lateral sclerosis**. Clinical Therapeutics 2015;37(3):668-680.	PURPOSE: Amyotrophic lateral sclerosis (ALS) is the most common motor neuron disease in adults. It is almost invariably lethal within a few years after the onset of symptoms. No effective treatment is currently available beyond supportive care and riluzole, a putative glutamate release blocker linked to modestly prolonged survival. This review provides a general overview of preclinical and clinical advances during recent years and summarizes the literature regarding emerging therapeutic approaches, focusing on their molecular targets. METHODS: A systematic literature review of PubMed was performed, identifying key clinical trials involving molecular therapies for ALS. In addition, the ALS Therapy Development Institute website was carefully analyzed, and a selection of ALS clinical trials registered at ClinicalTrials.gov has been included. FINDINGS: In the last several years, strategies have been developed to understand both the genetic and molecular mechanisms of ALS. Several therapeutic targets have been actively pursued, including kinases, inflammation inhibitors, silencing of key genes, and modulation or replacement of specific cell populations. The majority of ongoing clinical trials are investigating the safety profiles and tolerability of pharmacologic, gene, and cellular therapies, and have begun to assess their effects on ALS progression. IMPLICATIONS: Currently, no therapeutic effort seems to be efficient, but recent findings in ALS could help accelerate the discovery of an effective treatment for this disease.
2.	Gould RL, Coulson MC, Brown RG, Goldstein LH, Al-	Our objective was to systematically review and critically evaluate the evidence for psychotherapy and pharmacotherapy interventions for reducing distress or improving well-being in people with amyotrophic lateral sclerosis (pwALS). Online bibliographic

	Chalabi A, Howard RJ. **Psychotherapy and pharmacotherapy interventions to reduce distress or improve well-being in people with amyotrophic lateral sclerosis: A systematic review**. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 2015;16(5-6):293-302.	databases and clinical trial registers were searched and an assessment of study quality was conducted. Seven thousand two hundred and twenty-three studies were identified, of which five met inclusion criteria (four completed and one in progress). All studies examined psychotherapeutic interventions, and no studies investigated pharmacotherapy. Two studies adopted a randomized controlled trial design, one a controlled trial design and two a cohort design. Sample sizes were small in all studies (overall n = 145). The quality of completed studies was generally poor, with evidence that all were at potential risk of bias in numerous areas. Improvements in well-being were found with expressive disclosure (compared to no disclosure), cognitive behavioural therapy/counselling (compared to non-randomized pharmacotherapy) and hypnosis in the short term only, while no improvements were seen with a life review intervention. In conclusion, there is currently insufficient evidence to recommend the use of specific psychotherapy interventions for reducing distress or improving well-being in pwALS, and no evidence to support pharmacotherapy interventions. Research is urgently needed to address these significant gaps in the literature.
3.	Oliver D, Borasio GD, Voltz R, Caraceni A, De Visser M, Lorenzl S, et al. **The development of a consensus paper on palliative care in neurology-the implications for ALS care**. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 2014;15:117-118.	Background: A joint working group of the European Association for Palliative Care and the European Federation of Neurological Societies has produced a Consensus paper on the available evidence for the palliative care in progressive neurological disease. This has been a generic paper looking at all progressive neurological disease - including ALS/MND, multiple sclerosis, Parkinson ' s disease, stroke and primary brain tumours. The principles need to be considered separately for all disease groups as well - including ALS/ MND. Objectives: To show the important areas for consideration in the palliative care for people with ALS/MND. Methods: A literature search was undertaken including the main electronic databases and looking at the main areas of palliative care and neurology. Two investigators then looked at this literature, determined seven main areas and developed a draft list of papers. These were then commented on by a small group and then more widely until a consensus was developed. Results: The seven main areas all apply to the care of people with ALS/MND, and it could be argued that with the short prognosis of ALS/MND and the variable rate of progression this approach should be from the time of diagnosis. The areas of recommendation are: Palliative care should be considered early in the disease trajectory; the assessment and care should be provided by a multidisciplinary team approach, with access to specialist palliative care; communication should be open with patients and families and advance care planning is recommended. This should be as soon as possible in view of the likelihood of difficulties in communication and the development of cognitive change in ALS/MND; symptoms - physical and psychosocial - should be managed actively and appropriately; care needs should be assessed and carers supported before and after death. Professional carers should receive education, support and supervision to reduce the risks of emotional exhaustion; there should be repeated and continued discussion about end of life issues and discussion of patients ' wishes and aims. The recognition of the deterioration and dying phase will allow appropriate management and intervention; palliative care principles should be included with the training and continuing medical education of neurologists and palliative care professionals should understand the issues for neurological patients. Discussion and conclusion: The recommendations within the Consensus document can be seen to apply to the care of people with ALS/MND and there is a challenge to ensure that these principles are extended as widely as possible to support people with ALS/MND and their carers.

4.	Lee CN. **Reviewing evidences on the management of patients with motor neuron disease**. Hong Kong Medical Journal 2012;18(1):48-55.	OBJECTIVE: To review evidences on the management of patients with motor neuron disease. DATA SOURCES: PubMed literature searches from January 1982 up to January 2011. STUDY SELECTION: Key words for literature search were "motor neuron disease review (MND)". Only the articles which concentrated on the ventilation, nutrition, cognitive or multidisciplinary approaches for motor neuron disease were included. Case reports were not included in the review. In addition, publications were identified using the World Wide Web from references in these papers. Only articles in English were considered. DATA EXTRACTION: A total of 782 articles were retrieved using the key word search, of which 72 concentrated on ventilation, nutrition, cognitive or multidisciplinary approaches. From these, 43 articles were eventually included and formed the basis of this review. DATA SYNTHESIS: Motor neuron disease is an adult-onset neurodegenerative disease that leads to weakness of limb, bulbar, and respiratory muscles. It displays an ethnic variation in incidence; 90% of cases are sporadic and 10% are familial. New diagnostic criteria have been proposed to increase diagnostic sensitivity. Proper clinical studies, electrophysiology, and neuroimaging are necessary before reaching a diagnosis of motor neuron disease. Riluzole remains the only disease-modifying drug approved for this disease; it prolongs life by 3 to 4 months. Multidisciplinary care units are important in the management of motor neuron disease patients. Non-invasive positive pressure ventilation prolongs life in motor neuron disease patients with respiratory failure. Enteral feeding is usually recommended for affected patients with malnutrition. Cognitive impairment is common in these patients, for whom a formal neuropsychiatric assessment is recommended. Appropriate palliative care is needed for these patients in order to improve their quality of dying. CONCLUSION: Motor neuron disease is an incurable disease, for which a highly effective treatment is still pending. Symptomatic treatment remains the mainstay of management. A multidisciplinary approach embracing advances in non-invasive ventilation and gastrostomy can improve quality of life and extend the survival of motor neuron disease patients.
5.	Jia H, Xu YM. **Evidence-based evaluation of therapeutic measures for amyotrophic lateral sclerosis. [Chinese]**. Chinese Journal of Contemporary Neurology and Neurosurgery 2012;12(3):275-281.	Objective: To evaluate the therapeutic efficacy and side effects of various treatments for amyotrophic lateral sclerosis (ALS) in order to formulate the best therapeutic regimen. Methods: ALS, Riluzole, Gabapentin, Lamotrigine, neurotrophic factor, antioxidant and free radical scavenger gene therapy, neural stem cell treatment, treatment were appointed as retrieval words. MEDLINE, Cochrane Library, Wanfang Database for Scientific Journals in China and Chinese National Knowledge Infrastructure (CNKI) for Scientific Journals Database were used for retrieval. Related clinical guidelines, systematic reviews, randomised controlled trials, controlled clinical trials and case-observation studies were collected following the corresponding inclusion criteria and exclusion criteria and evaluated by Jadad Scale to judge the authenticity and reliability of the conclusion. Manual searching was also used. Results: After screening, 39 related articals were selected as follow: 4 systematic reviews, 18 randomised controlled trials, 11 controlled clinical trials, and 6 case-observation studies. Twenty-seven articals were of high quality (according to Jadad Scale, 11 with

		score 4, 13 with score 5, and 3 with score 7), while 12 were of low quality with score 3. According to the evaluation of therapeutic efficacy and side effects of various therapies, it is suggested that: 1) The Riluzole is the only drug approved by American FDA, lacking of more effective treatments. 2) When the patients' condition is not relieved, medicine-combined therapies and symptomatic treatments should be used. Conclusion: Evidence-based medicine can provide best clinical evidence on ALS treatment.
6.	Fonseca LA, Fontes SV, Anequini IP, Favero FM, Oliveira ASB. **Emergency guidelines for professionals who treat patients with amyotrophic lateral sclerosis**. Revista Neurociencias 2012;20(2):260-265.	Objective. This article attempts a literature review of guidelines on emergency Amyotrophic lateral sclerosis (ALS) for health professionals. Method. We conducted a literature review and the last ten years. We searched in the databases LILACS, SciELO, MEDLINE, PEDRO and PUBMED articles of the systematic review, guidelines, manuals associations, electronic documents and other studies. Results. Most of the manuals found address changes that can be observed in patients with ALS as sleep disorders, ulcers and skin lesions, drooling, dysarthria, dysphagia, but does not emphasize the procedures to be taken by health professionals when their patients have such symptoms, other essential items in the emergency care of patients with ALS as: caring for the oxygenation of these patients, invasive mechanical ventilation, tracheostomy, weaning, among others. Conclusion. Through the research in question was found that the literature is scarce and it is suggested the elaboration of a comprehensive emergency guide book that addresses the primary care that health professionals should perform in an emergency situation in the hospital or at home.
7.	Diagnosis ETFo, Management of Amyotrophic Lateral S, Andersen PM, Abrahams S, Borasio GD, de Carvalho M, et al. **EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS)--revised report of an EFNS task force**. European Journal of Neurology 2012;19(3):360-375.	BACKGROUND: The evidence base for the diagnosis and management of amyotrophic lateral sclerosis (ALS) is weak. OBJECTIVES: To provide evidence-based or expert recommendations for the diagnosis and management of ALS based on a literature search and the consensus of an expert panel. METHODS: All available medical reference systems were searched, and original papers, meta-analyses, review papers, book chapters and guidelines recommendations were reviewed. The final literature search was performed in February 2011. Recommendations were reached by consensus. RECOMMENDATIONS: Patients with symptoms suggestive of ALS should be assessed as soon as possible by an experienced neurologist. Early diagnosis should be pursued, and investigations, including neurophysiology, performed with a high priority. The patient should be informed of the diagnosis by a consultant with a good knowledge of the patient and the disease. Following diagnosis, the patient and relatives/carers should receive regular support from a multidisciplinary care team. Medication with riluzole should be initiated as early as possible. Control of symptoms such as sialorrhoea, thick mucus, emotional lability, cramps, spasticity and pain should be attempted. Percutaneous endoscopic gastrostomy feeding improves nutrition and quality of life, and gastrostomy tubes should be placed before respiratory insufficiency develops. Non-invasive positive-pressure ventilation also improves survival and quality of life. Maintaining the patient's ability to communicate is essential. During the entire course of the disease, every effort should be made to maintain patient autonomy. Advance directives for palliative end-of-life care should be discussed early with the patient and carers, respecting the patient's social and cultural background.

8.	Andersen PM, Abrahams S, Borasio GD, de Carvalho M, Chio A, Van Damme P, et al. **EFNS guidelines on the Clinical Management of Amyotrophic Lateral Sclerosis (MALS) - revised report of an EFNS task force**. European Journal of Neurology 2012;19(3):360-375.	Background: The evidence base for the diagnosis and management of amyotrophic lateral sclerosis (ALS) is weak. Objectives: To provide evidence-based or expert recommendations for the diagnosis and management of ALS based on a literature search and the consensus of an expert panel. Methods: All available medical reference systems were searched, and original papers, meta-analyses, review papers, book chapters and guidelines recommendations were reviewed. The final literature search was performed in February 2011. Recommendations were reached by consensus. Recommendations: Patients with symptoms suggestive of ALS should be assessed as soon as possible by an experienced neurologist. Early diagnosis should be pursued, and investigations, including neurophysiology, performed with a high priority. The patient should be informed of the diagnosis by a consultant with a good knowledge of the patient and the disease. Following diagnosis, the patient and relatives/carers should receive regular support from a multidisciplinary care team. Medication with riluzole should be initiated as early as possible. Control of symptoms such as sialorrhoea, thick mucus, emotional lability, cramps, spasticity and pain should be attempted. Percutaneous endoscopic gastrostomy feeding improves nutrition and quality of life, and gastrostomy tubes should be placed before respiratory insufficiency develops. Non-invasive positive-pressure ventilation also improves survival and quality of life. Maintaining the patient's ability to communicate is essential. During the entire course of the disease, every effort should be made to maintain patient autonomy. Advance directives for palliative end-of-life care should be discussed early with the patient and carers, respecting the patient's social and cultural background. © 2011 The Author(s). European Journal of Neurology © 2011 EFNS.
9.	Flynn K. **Systematic Reviews for Amyotrophic Lateral Sclerosis**. Boston: VATAP, VA Technology Assessment Program; 2010. (INAHTA Briefs Issue 2010/061).	To summarize the literature on amyotrophic lateral sclerosis (ALS) in support of the National Task Group's development of an integrated system of care for veterans with ALS. http://www.inahta.org/upload/Briefs_11/10061_VATAP_Systemati_Reviews_Amyotrophic_Lateral_Sclerosis.pdf
10.	Benatar M, Kurent J, Moore DH. **Treatment for familial amyotrophic lateral sclerosis/motor neuron disease**. Cochrane Database of Systematic Reviews 2009;(1):CD006153.	Background: Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease (MND), is a rare neurodegenerative disease. Approximately 5% to 7% of ALS/MND patients report a family history of a similarly affected relative. Superoxide dismutase-1 gene mutations are the cause in about 20% of familial cases. In those with non-familial (sporadic) ALS/MND the cause is unknown. Also unknown is whether patients with familial and sporadic ALS/MND respond differently to treatment. Objectives: To systematically review the literature and to answer the specific question: 'Is there a difference in the response to treatment between patients with sporadic and familial forms of ALS?' Search strategy: In May 2006 we searched the Cochrane Neuromuscular Disease Group Trials Register, MEDLINE (January 1966 to May 2006) and EMBASE (January 1980 to May 2006) for randomized

		controlled trials (RCTs). Two review authors read the titles and abstracts of all articles and reviewed the full text of all possibly relevant articles. We scanned references of all included trials to identify additional relevant articles. For all trials eligible for inclusion we contacted the authors to request the necessary raw data. Selection criteria: Studies had to meet two criteria: (a) randomized controlled study design, and (b) inclusion of patients with both familial and sporadic ALS/MND. Data collection and analysis: We attempted to contact authors of all trials that met inclusion criteria. We obtained data regarding ALS/MND type (sporadic versus familial), treatment assignment (active versus placebo), survival and ALS Functional Rating Scale scores for four large RCTs that included 822 sporadic and 41 familial ALS patients. We could not obtain data from 25 potentially eligible studies (17 trial authors could not be contacted and eight were unwilling to provide data). There was no statistical evidence for a different response to treatment in patients with familial ALS/MND compared to those with sporadic ALS/MND. The pooled estimate of the hazard ratio for the interaction term (treatment x familial ALS) suggested a more beneficial response with respect to survival among patients with familial ALS/MND, but the result was not statistically significant. Estimates of the rate of decline on the ALS Functional Rating Scale also suggested a slightly better response to treatment among those with familial ALS/MND, but the result was not statistically significant. Authors' conclusions: Future RCTs should document whether patients with familial ALS/MND are included and the presence or absence of a mutation in the superoxide dismutase-1 gene amongst those with familial ALS/MND. © 2009 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
11.	Miller RG. **Practice parameter update: The care of the patient with amyotrophic lateral sclerosis: Drug, nutritional, and respiratory therapies (An evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology.** Neurology 2009;73(15):1218-1226.	BJECTIVE: To systematically review evidence bearing on the management of patients with amyotrophic lateral sclerosis (ALS). METHODS: The authors analyzed studies from 1998 to 2007 to update the 1999 practice parameter. Topics covered in this section include slowing disease progression, nutrition, and respiratory management for patients with ALS. RESULTS: The authors identified 8 Class I studies, 5 Class II studies, and 43 Class III studies in ALS. Important treatments are available for patients with ALS that are underutilized. Noninvasive ventilation (NIV), percutaneous endoscopic gastrostomy (PEG), and riluzole are particularly important and have the best evidence. More studies are needed to examine the best tests of respiratory function in ALS, as well as the optimal time for starting PEG, the impact of PEG on quality of life and survival, and the effect of vitamins and supplements on ALS. RECOMMENDATIONS: Riluzole should be offered to slow disease progression (Level A). PEG should be considered to stabilize weight and to prolong survival in patients with ALS (Level B). NIV should be considered to treat respiratory insufficiency in order to lengthen survival (Level B) and to slow the decline of forced vital capacity (Level B). NIV may be considered to improve quality of life (Level C) [corrected].Early initiation of NIV may increase compliance (Level C), and insufflation/exsufflation may be considered to help clear secretions (Level C).
12.	Zoccolella S, Santamato A, Lamberti P. **Current and emerging treatments for**	BACKGROUND: Amyotrophic lateral sclerosis (ALS) is a relatively rare neurodegenerative disorder of both upper and lower motoneurons. Currently, the management of ALS is essentially symptoms-based, and riluzole, an antiglutamatergic agent, is the only drug for the treatment of ALS approved by the food and drug administration.

	amyotrophic lateral sclerosis. Neuropsychiatric Disease & Treatment 2009;5:577-595.	OBJECTIVE: We reviewed current literature concerning emerging treatments for amyotrophic lateral sclerosis. METHODS: A Medline literature search was performed to identify all studies on ALS treatment published from January 1st, 1986 through August 31st, 2009. We selected papers concerning only disease-modifying therapy. RESULTS: Forty-eight compounds were identified and reviewed in this study. CONCLUSIONS: Riluzole is the only compound that demonstrated a beneficial effect on ALS patients, but with only modest increase in survival. Although several drugs showed effective results in the animal models for ALS, none of them significantly prolonged survival or improved quality of life of ALS patients. Several factors have been implicated in explaining the predominantly negative results of numerous randomized clinical trials in ALS, including methodological problems in the use of animal-drug screening, the lack of assessment of pharmacokinetic profile of the drugs, and methodological pitfalls of clinical trials in ALS patients.
13.	Miller RG, Jackson CE, Kasarskis EJ, England JD, Forshew DA, Johnston W, et al. **Aan practice parameter update: The care of the patient with amyotrophic lateral sclerosis (an evidence-based review)**. Amyotrophic Lateral Sclerosis 2009;10:12-13.	Background: The American Academy of Neurology (AAN) issued an evidence-based report on managing patients with amyotrophic lateral sclerosis (ALS) in 1999. Objective: To systematically review evidence bearing on the management of patients with ALS and update the 1999 AAN practice parameter. Methods: The authors completed a systematic literature review from 1998 to 2008. Topics included breaking the news, symptom management, slowing disease progression, nutrition, respiratory management, palliative care, cognitive and behavioral impairment, multidisciplinary clinics, and communication for patients with ALS. Results: The authors identified 10 Class I studies, 13 Class II studies, and 73 Class III studies in ALS. More studies are clearly needed to examine the best tests of respiratory function in ALS, the optimal time for starting PEG, the impact of PEG on quality of life and survival, the effect of vitamins and supplements, symptomatic therapies and palliative care. The following recommendations are made based on the studies analyzed: Riluzole should be offered to slow disease progression (Level A). Percutaneous endoscopic gastrostomy (PEG) should be considered to stabilize weight and to prolong survival (Level B). Noninvasive ventilation (NIV) should be considered to treat respiratory insufficiency in order to lengthen survival (Level B), and may be considered to slow the decline of forced vital capacity (Level C) and improve quality of life (Level C). Early initiation of NIV may increase compliance (Level C), and insufflation/exsufflation may be considered to help clear secretions (Level C). Multidisciplinary clinic referral should be considered to optimize health care delivery and prolong survival (Level B) and may be considered to enhance quality of life (Level C). For the treatment of refractory sialorrhea, botulinum toxin B should be considered (Level B) and low-dose radiation therapy to the salivary glands may be considered (Level C). For treatment of pseudobulbar affect, the combination therapy of dextro-methorphan with quinidine should be considered, though side effects are not uncommon and the treatment is currently not approved by the U.S. Food and Drug Administration (Level B). For patients who develop fatigue while taking riluzole, withholding the drug may be considered (Level C). Because many patients with ALS demonstrate cognitive impairment, which in some cases meets criteria for dementia, screening for cognitive and behavioral impairment should be considered in patients with ALS (Level B). Other management strategies all lack strong evidence. Discussion: There are many treatments available for patients with ALS that can alleviate suffering. NIV, PEG, riluzole, and multidisciplinary clinics are the most important and have the best evidence. Conclusions: More high-quality, controlled studies are needed to guide management and to assess outcomes in patients with ALS.

14. Miller RG, Jackson CE, Kasarskis EJ, England JD, Forshew D, Johnston W, et al. **Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology**. Neurology 2009;73(15):1218-1226.	OBJECTIVE: To systematically review evidence bearing on the management of patients with amyotrophic lateral sclerosis (ALS). METHODS: The authors analyzed studies from 1998 to 2007 to update the 1999 practice parameter. Topics covered in this section include slowing disease progression, nutrition, and respiratory management for patients with ALS. RESULTS: The authors identified 8 Class I studies, 5 Class II studies, and 43 Class III studies in ALS. Important treatments are available for patients with ALS that are underutilized. Noninvasive ventilation (NIV), percutaneous endoscopic gastrostomy (PEG), and riluzole are particularly important and have the best evidence. More studies are needed to examine the best tests of respiratory function in ALS, as well as the optimal time for starting PEG, the impact of PEG on quality of life and survival, and the effect of vitamins and supplements on ALS. RECOMMENDATIONS: Riluzole should be offered to slow disease progression (Level A). PEG should be considered to stabilize weight and to prolong survival in patients with ALS (Level B). NIV should be considered to treat respiratory insufficiency in order to lengthen survival (Level B) and to slow the decline of forced vital capacity (Level B). NIV may be considered to improve quality of life (Level C) [corrected].Early initiation of NIV may increase compliance (Level C), and insufflation/exsufflation may be considered to help clear secretions (Level C).
15. Miller RG, Jackson CE, Kasarskis EJ, England JD, Forshew D, Johnston W, et al. **Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology**. Neurology 2009;73(15):1227-1233.	OBJECTIVE: To systematically review evidence bearing on the management of patients with amyotrophic lateral sclerosis (ALS). METHODS: The authors analyzed studies from 1998 to 2007 to update the 1999 practice parameter. Topics covered in this section include breaking the news, multidisciplinary clinics, symptom management, cognitive and behavioral impairment, communication, and palliative care for patients with ALS. RESULTS: The authors identified 2 Class I studies, 8 Class II studies, and 30 Class III studies in ALS, but many important areas have been little studied. More high-quality, controlled studies of symptomatic therapies and palliative care are needed to guide management and assess outcomes in patients with ALS. RECOMMENDATIONS: Multidisciplinary clinic referral should be considered for managing patients with ALS to optimize health care delivery and prolong survival (Level B) and may be considered to enhance quality of life (Level C). For the treatment of refractory sialorrhea, botulinum toxin B should be considered (Level B) and low-dose radiation therapy to the salivary glands may be considered (Level C). For treatment of pseudobulbar affect, dextromethorphan and quinidine should be considered if approved by the US Food and Drug Administration (Level B). For patients who develop fatigue while taking riluzole, withholding the drug may be considered (Level C). Because many patients with ALS demonstrate cognitive impairment, which in some cases meets criteria for dementia, screening for cognitive and behavioral impairment should be considered in patients with ALS (Level B). Other management strategies all lack strong evidence.

16. Kollewe K, Andersen P, Borasio G, Hardiman O, Leigh P, Pradat P, et al. **Good practice in the management of amyotrophic lateral sclerosis: Clinical guidelines An evidencebased review with good practice points from the EALSC working group**. Nervenheilkunde: Zeitschrift fur interdisziplinaere Fortbildung 2008;27(4):302-316.	The evidence base for diagnosis and management of Amyotrophic Lateral Sclerosis (ALS) is still weak, and curative therapy is lacking. Nonetheless, early diagnosis and symptomatic and therapy can profoundly influence care and quality of life of the patient and relatives, and may increase survival time. This review addresses the current optimal clinical approach to ALS. The literature search is complete to December 2006. Where there was lack of evidence but consensus was clear we have stated our opinion as good practice points. We conclude that a diagnosis of ALS can be achieved by early examination by an experienced neurologist. The patient should be informed of the diagnosis by the consultant. Following diagnosis, a multi-disciplinary care team should support the patient and relatives. Medication with riluzole should be initiated as early as possible. Percutaneous endocopic gastrostomy (PEG) is associated with improved nutrition and should be inserted early. Non-invasive positive pressure ventilation improves survival and quality of life but is underused in Europe. Maintaining the patient's ability to communicate is essential. During the course of the disease, every effort should be made to maintain patient autonomy. Advance directives for palliative end of life care are important and should be discussed early with the patient and relatives if they so wish. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract).
17. Andersen PM, Borasio GD, Dengler R, Hardiman O, Kollewe K, Leigh PN, et al. **Good practice in the management of amyotrophic lateral sclerosis: clinical guidelines. An evidence-based review with good practice points. EALSC Working Group**. Amyotrophic Lateral Sclerosise 2007;8(4):195-213.	The evidence base for diagnosis and management of ALS is still weak, and curative therapy is lacking. Nonetheless, early diagnosis and symptomatic therapy can profoundly influence care and quality of life of the patient and relatives, and may increase survival time. This review addresses the current optimal clinical approach to ALS. The literature search is complete to December 2006. Where there was lack of evidence but consensus was clear we have stated our opinion as good practice points. We conclude that a diagnosis of ALS can be achieved by early examination by an experienced neurologist. The patient should be informed of the diagnosis by the consultant. Following diagnosis, a multi-diciplinary care team should support the patient and relatives. Medication with riluzole should be initiated as early as possible. PEG is associated with improved nutrition and should be inserted early. The operation is hazardous in patients with VC <50%: RIG may be a better alternative. Non-invasive positive pressure ventilation improves survival and quality of life but is underused in Europe. Maintaining the patient's ability to communicate is essential. During the course of the disease, every effort should be made to maintain patient autonomy. Advance directives for palliative end of life care are important and should be discussed early with the patient and relatives if they so wish.
18. Shoesmith CL, Strong MJ. **Amyotrophic lateral sclerosis: update for family physicians**. Canadian Family Physician 2006;52(12):1563-1569.	OBJECTIVE: To discuss the epidemiology, pathogenesis, diagnosis, expected course, prognosis, and treatment of amyotrophic lateral sclerosis (ALS), a degenerative disorder of the nervous system associated with progressive weakness. QUALITY OF EVIDENCE: PubMed and the Cochrane Database of Systematic Reviews were searched using the MeSH headings "amyotrophic lateral sclerosis," "therapy," "epidemiology," and "etiology." Articles containing the best available evidence were reviewed. Most provided level II and III evidence. There were some level I drug trials.

		MAIN MESSAGE: Amyotrophic lateral sclerosis is associated with progressive dysarthria, dysphagia, and weakness in the extremities. Diagnosis is based on physical examination, electrophysiology, and excluding other confounding conditions. There is no cure for this devastating disorder. Certain treatments, however, can improve survival and quality of life. CONCLUSION: Because ALS is a complex disease, care of ALS patients is best provided at multidisciplinary clinics that specialize in managing patients with this disorder.
19.	Mitsumoto H, Bromberg M, Johnston W, Tandan R, Byock I, Lyon M, et al. **Promoting excellence in end-of-life care in ALS**. Amyotrophic Lateral Sclerosis & Other Motor Neuron Disorders 2005;6(3):145-154.	The type and quality of end-of-life care varies greatly in ALS; the time to initiate end-of-life care is not defined, and decision making is hampered by logistical and financial barriers. There has been no systematic review of these issues in ALS. The goals of this initiative are to: 1) improve end-of-life care for patients with ALS and families based on what limited evidence is available; 2) increase awareness, interest, and debate on the end-of-life care in ALS; and 3) identify areas needed for new prospective clinical research. The ALS Peer Workgroup reviewed the literature and 1) identified the current state of knowledge, 2) analysed the gaps in care, and 3) provided recommendations for standard of care and future research. It was shown that areas of investigation are needed on the incorporation of an interdisciplinary approach to care in ALS that includes: psychosocial evaluation and spiritual care; the use of validated instruments to assess patient and caregiver quality of life; and the establishment of proactive caregiver programs. Several public policy changes that will improve coverage for medical care, hospice, and caregiver costs are also reviewed. More clinical evidence is needed on how to provide optimal end-of-life care specifically in ALS.
20.	Andersen PM, Borasio GD, Dengler R, Hardiman O, Kollewe K, Leigh PN, et al. **EFNS task force on management of amyotrophic lateral sclerosis: guidelines for diagnosing and clinical care of patients and relatives**. European Journal of Neurology 2005;12(12):921-938.	Despite being one of the most devastating diseases known, there is little evidence for diagnosing and managing patients with amyotrophic lateral sclerosis (ALS). Although specific therapy is lacking, correct early diagnosis and introduction of symptomatic and specific therapy can have a profound influence on the care and quality of life of the patient and may increase survival time. This document addresses the optimal clinical approach to ALS. The final literature search was performed in the spring of 2005. Consensus recommendations are given graded according to the EFNS guidance regulations. Where there was lack of evidence but consensus was clear we have stated our opinion as good practice points. People affected with possible ALS should be examined as soon as possible by an experienced neurologist. Early diagnosis should be pursued and a number of investigations should be performed with high priority. The patient should be informed of the diagnosis by a consultant with a good knowledge of the patient and the disease. Following diagnosis, the patient and relatives should receive regular support from a multidisciplinary care team. Medication with riluzole should be initiated as early as possible. PEG is associated with improved nutrition and should be inserted early. The operation is hazardous in patients with vital capacity < 50%. Non-invasive positive pressure ventilation improves survival and quality of life but is underused. Maintaining the patients ability to communicate is essential. During the entire course of the disease, every effort should be made to maintain patient autonomy. Advance directives for palliative end of life care are important and should be fully discussed early with the patient and relatives respecting the patients social and cultural background.

21.	Miller RG. **Examining the evidence about treatment in ALS/MND**. Amyotrophic Lateral Sclerosis & Other Motor Neuron Disorders 2001;2(1):3-7.	The application of evidence-based medicine to the treatment of patients with amyotrophic lateral sclerosis (ALS) is just beginning. A small number of systematic reviews analyzing the pertinent evidence, grading the methodology and formulating recommendations to guide clinical decision-making have begun to appear. The American Academy of Neurology practice parameters for informing the patient and managing nutritional and respiratory issues and palliative care are discussed. In addition, the first systematic review in the field of ALS/MND from the Cochrane collaboration concerns riluzole treatment and this meta-analysis is also described. Some of the most important recommendations that have the potential to significantly prolong survival and enhance quality of life are the early institution of percutaneous endoscopic gastrostomy for patients with significant dysphagia, and the initiation of non-invasive positive pressure ventilation for patients with symptoms of early respiratory insufficiency. Assertive treatment of pain and dyspnea are also strongly recommended for patients with ALS. The North American ALS patient database, ALS C.A.R.E., is also described as a methodology for measuring clinical outcomes, and some early results are presented. The evidence on riluzole indicates effectiveness in prolonging survival with a good safety profile.

Akupunktur

Tab. 2: Systematiske oversikter om effekten av akupunktur

	Referanse	Sammendrag
1.	Park HJ, Park J, Kim MJ, Hong M, Yang J, Choi S, et al. **Acupuncture application for neurological disorders**. Neurological Research 2007;29(SUPPL. 1):S49-S54.	Background: Acupuncture has been widely used for a range of neurological disorders. Despite its popularity, the evidence to support the use of acupuncture is contradictory. Methods: This review was designed to summarize and to evaluate the available evidence of acupuncture for neurological disorders. Results: Most of the reviewed studies suffer from lack of methodological rigor. Owing to paucity and poor quality of the primary studies, no firm conclusion could be drawn on the use of acupuncture for epilepsy, Alzheimer's disease, Parkinson's disease, ataxic disorders, multiple sclerosis, amyotrophic lateral sclerosis and spinal cord injury. For stroke rehabilitation, the evidence from recent high-quality trials and previous systematic reviews is not convincing. Conclusion: More rigorous trials are warranted to establish acupuncture's role in neurological disorders. © 2007 W. S. Maney & Son Ltd.
2.	Sun H, Cui LY. **Temporary state of acupuncture treat-**	Objective: To review systemically the literatures about acupuncture for treatment of motor neuron disease so as to provide relative data for clinic, and discuss a new strategy for development of acupuncture therapy for motor neuron disease. Data sources: Using the key terms "motor neuron disease, acupuncture", we searched http://www.chkd.cnki.net from 1994 to 2003 in range of

	ment of motor neuron disease. [Chinese]. Chinese Journal of Clinical Rehabilitation 2005;9(21):174-175.	Chinese Medical Key Journals. Study selection: A total of 100 articles related to the treatment of acupuncture in motor neuron disease. Data extraction: Among the 100 articles, 53 met inclusion criteria, 15 of which were selected as reference literature. Data synthesis: From point of view of Traditional Chinese Medicine, motor neuron disease belonged to Wei-Syndrome. On Traditional Chinese Medicine theory of replenishing spleen, invigorating kidney and liver, treatment of motor neuron disease with acupuncture had obtained some efficacy in clinic. In clinic, scalp or body puncturing was usually applied, often with point injection. However, most reports had many problems including the lack of strict scientific design, randomized controls, unite standard for evaluation of curative effect, follow up and insufficient samples, so the effect of acupuncture therapy for motor neuron disease needed further research. Conclusion: Acupuncture therapy has a certain efficacy in treating motor neuron disease, but large-sample randomized controlled trial is required to evaluate the true efficacy of acupuncture in treatment of motor neuron disease so that we can find an effective treatment with acupuncture in clinic.

Ernæring

Tab. 3: Systematiske oversikter om effekten av ulike ernæringstiltak

	Referanse	Sammendrag
1.	Gomes Jr Claudio AR, Andriolo Régis B, Bennett C, Lustosa Suzana AS, Matos D, Waisberg Daniel R, et al. **Percutaneous endoscopic gastrostomy versus nasogastric tube feeding for adults with swallowing disturbances**. Cochrane Database of Systematic Reviews 2015 (5):CD008096.	Background: A number of conditions compromise the passage of food along the digestive tract. Nasogastric tube (NGT) feeding is a classic, time-proven technique, although its prolonged use can lead to complications such as lesions to the nasal wing, chronic sinusitis, gastro-oesophageal reflux, and aspiration pneumonia. Another method of infusion, percutaneous endoscopy gastrostomy (PEG), is generally used when there is a need for enteral nutrition for a longer time period. There is a high demand for PEG in patients with swallowing disorders, although there is no consistent evidence about its effectiveness and safety as compared to NGT.Objectives: To evaluate the effectiveness and safety of PEG compared with NGT for adults with swallowing disturbances.Search methods: We searched The Cochrane Library, MEDLINE, EMBASE, and LILACS from inception to January 2014, and contacted the main authors in the subject area. There was no language restriction in the search.Selection criteria: We planned to include randomised controlled trials comparing PEG versus NGT for adults with swallowing disturbances or dysphagia and indications for nutritional support, with any underlying diseases. The primary outcome was intervention failure (e.g. feeding interruption, blocking or leakage of the tube, no adherence to treatment).Data collection and analysis: We used standard methodological procedures expected by The

Cochrane Collaboration. For dichotomous and continuous variables, we used risk ratio (RR) and mean difference (MD), respectively with the random-effects statistical model and 95% confidence interval (CI). We assumed statistical heterogeneity when I^2 > 50%.Main results: We included 11 randomised controlled studies with 735 participants which produced 16 meta-analyses of outcome data. Meta-analysis indicated that the primary outcome of intervention failure, occurred in lower proportion of participants with PEG compared to NGT (RR 0.18, 95% CI 0.05 to 0.59, eight studies, 408 participants, low quality evidence) and this difference was statistically significant. For this outcome, we also subgrouped the studies by endoscopic gastrostomy technique into pull, and push and not reported. We observed a significant difference favouring PEG in the pull subgroup (RR 0.07, 95% CI 0.01 to 0.35, three studies, 90 participants). Thepush subgroup contained only one clinical trial and the result favoured PEG (RR 0.05, 95% CI 0.00 to 0.74, one study, 33 participants) techniques. We found no statistically significant difference in cases where the technique was not reported (RR 0.43, 95% CI 0.13 to 1.44, four studies, 285 participants).There was no statistically significant difference between the groups for meta-analyses of the secondary outcomes of mortality (RR 0.86, 95% CI 0.58 to 1.28, 644 participants, nine studies, very low quality evidence), overall reports of any adverse event at any follow-up time point (ITT analysis, RR 0.83, 95% CI 0.51 to 1.34), 597 participants, 6 studies, moderate quality evidence), specific adverse events including pneumonia (aspiration) (RR 0.70, 95% CI 0.46 to 1.06, 645 participants, seven studies, low quality evidence), or for the meta- analyses of the secondary outcome of nutritional status including weight change from baseline, and mid-arm circumference at endpoint, although there was evidence in favour of PEG for meta-analyses of mid-arm circumference change from baseline (MD 1.16, 95% CI 1.01 to 1.31, 115 participants, two studies), and levels of serum albumin were higher in the PEG group (MD 6.03, 95% CI 2.31 to 9.74, 107 participants).For meta-analyses of the secondary outcomes of time on enteral nutrition, there was no statistically significant difference (MD 14.48, 95% CI -2.74 to 31.71; 119 participants, two studies). For meta-analyses of quality of life measures (EuroQol) outcomes in two studies with 133 participants, for inconvenience (RR 0.03, 95% CI 0.00 to 0.29), discomfort (RR 0.03, 95% CI 0.00 to 0.29), altered body image (RR 0.01, 95% CI 0.00 to 0.18; P = 0.001) and social activities (RR 0.01, 95% CI .00 to 0.18) the intervention favoured PEG, that is, fewer participants found the intervention of PEG to be inconvenient, uncomfortable or interfered with social activities. However, there were no significant differences between the groups for pain, ease of learning to use, or the secondary outcome of length of hospital stay (two studies, 381 participants).Authors' conclusions: PEG was associated with a lower probability of intervention failure, suggesting the endoscopic procedure may be more effective and safe compared with NGT. There is no significant difference in mortality rates between comparison groups, or in adverse events, including pneumonia related to aspiration. Future studies should include details of participant demographics including underlying disease, age and gender, and the gastrostomy technique.

2.	Stavroulakis T, Walsh T, Shaw PJ, McDermott CJ, Progas S. **Gastrostomy use in motor neurone disease (MND): a review, meta-analysis and survey of current practice**. Amyotrophic Lateral sclerosis & Frontotemporal Degeneration 2013;14(2):96-104.	Abstract Gastrostomy feeding is commonly used to support MND patients with dysphagia. In this paper we review three main methods of gastrostomy insertion (PEG, RIG, PIG); conduct a meta-analysis of mortality data following gastrostomy; and present a survey of current practice. A review of the literature revealed a lack of high quality evidence to indicate the optimal method and timing for gastrostomy insertion in patients with MND. A survey of 20 MND clinics demonstrated a clinic-based variability of gastrostomy practices due to factors such as clinician preference, availability of method, and patient respiratory function. The meta-analysis demonstrated that the estimate of the absolute difference in mortality rates was 2.1% higher for PEG (- 6.3%, + 11.2%), suggesting that RIG and PIG methods may be safer than PEG. These results and observations highlight the need for more research to evaluate and compare the safety of the differerent gastrostomy insertion methods in MND care.
3.	Katzberg HD, Benatar M. **Enteral tube feeding for amyotrophic lateral sclerosis/motor neuron disease**. Cochrane Database of Systematic Reviews 2011 (1):CD004030.	BACKGROUND: Enteral feeding (tube feeding) is offered to many people with amyotrophic lateral sclerosis/motor neuron disease experiencing difficulty swallowing (dysphagia) and maintaining adequate nutritional intake leading to weight loss. OBJECTIVES: To examine the efficacy of percutaneous endoscopic gastrostomy placement or other tube feeding placement on: (1) survival;(2) nutritional status; (3) quality of life;(4) minor and major complications of percutaneous endoscopic gastrostomy. SEARCH STRATEGY: We searched the Cochrane Neuromuscular Disease Group Trials Register (24 November 2009), MEDLINE (from January 1966 to September 2009), and EMBASE (from January 1980 to September 2009) for all papers on enteral tube feeding in amyotrophic lateral sclerosis/motor neuron disease. The results were screened to identify randomised controlled trials and to identify non-randomized studies that might be worthy of review and discussion. We checked references in published articles and enlisted personal communications to identify any additional references. SELECTION CRITERIA: A priori selection criteria included randomised and quasi-randomized controlled trials evaluating the efficacy of percutaneous endoscopic gastrostomy or other feeding tube placement. Since no such trials were discovered, all prospective and retrospective controlled studies were reviewed in the 'Background' or 'Discussion' sections of the review. DATA COLLECTION AND ANALYSIS: We independently assessed study design and extracted data. We considered the following outcomes: (1) survival rate in months (of primary interest), (2) nutritional status measured by weight change, change in body mass index, or other quantitative index of nutritional status, (3) self-perceived quality of life and (4) safety of the procedure as indicated by minor and major complications of surgical or radiological guided PEG tube insertion.

		MAIN RESULTS: We found no randomised controlled trials comparing the efficacy of enteral tube feeding with those people who continued to eat orally, without enteral feeding. We summarized the results of retrospective and prospective studies in the 'Discussion' section. AUTHORS' CONCLUSIONS: There are no randomised controlled trials to indicate whether enteral tube feeding is beneficial compared to continuation of oral feeding for any of the outcome measures. The 'best' evidence to date suggests a survival advantage for some people with amyotrophic lateral sclerosis/motor neuron disease, but these conclusions are tentative. Evidence for improved nutrition is also incomplete but tentatively favorable. Quality of life has been addressed in studies and needs more attention. Based on a number of recent non-randomized studies comparing surgical and radiographic approaches to feeding tube insertion these two procedures for PEG tube insertion appear to be equivalent.
4.	Van Den Berg JP, Wijnen C. **Guideline for nutritional care in ALS**. Amyotrophic Lateral Sclerosis 2009;10:181.	Background: Most Dutch multidisciplinary ALS treatment teams have implemented the protocol for rehabilitative management in ALS (1). Although the ability to eat and drink are two of the most important functions in life and the progressive loss of these abilities has an immense impact on the patients and their families, the dietician was not always an integral member of the treatment team (2). It is known that optimal nutritional management by a dietician can positively influence survival and quality of life, but detailed evidence-based information for dieticians is lacking. Objectives: To obtain a nutritional guideline in order to equip dieticians in helping to provide optimal nutritional care for ALS patients. Methods: A guideline has been developed by reviewing the literature, in combination with practice-based experience from ALS dieticians. The guideline (3) has been written by Dieticians for Neuromuscular Diseases, an officially registered group of the Dutch Association of Dieticians. Results: The guideline was published in the autumn of 2007. It is the initial step toward developing a national nutritional policy, for which the implementation continues. Discussion and Conclusions: The guideline is a an instrument to initiate national and international discussion considering the statements of preventing weight gain, energy requirements influenced by progression and weight evolution, protein requirements, use of fibres during the course of the disease and defining palliative nutrition. Presentation of the statements will lead to discussion and establishing consensus on the nutritional requirements of ALS patients.
5.	Ballesteros Pomar MD, Ares Luque A. **Evidence-based nutrition in neurological diseases. [Spanish].** Endocrinologia y Nutricion 2005;52(SUPPL.	Neurological disease causes considerable morbidity in developed countries and frequently leads to alterations in the level of consciousness or in the mechanisms of swallowing, which may necessitate artificial nutritional support. The present review aims to evaluate nutritional support in acute cerebral vascular disease, dementia and amyotrophic lateral sclerosis, as well as the utility of a ketogenic diet in the treatment of epilepsy, based on the best available scientific evidence. A literature search was performed in Medline (PubMed) and in the

	2):97-101.	Cochrane Library Plus in Spanish. Randomized clinical studies, systematic reviews, and meta-analyses were selected. There are few prospective randomized studies on nutritional support in neurological diseases. The FOOD study shows that the nasogastric tube is a better route of administration than percutaneous endoscopic gastrostomy for enteral nutrition in the first month after stroke. In the case of dementia and other neurodegenerative diseases, the available evidence is weak. There are no reliable data from randomized controlled trials that support the use of ketogenic diets in patients with epilepsy.
6.	Heffernan C, Jenkinson C, Holmes T, Feder G, Kupfer R, Leigh PN, et al. **Nutritional management in MND/ALS patients: an evidence based review**. Amyotrophic Lateral Sclerosis & Other Motor Neuron Disorders 2004;5(2):72-83.	Sammendrag ikke tilgjengelig

Fysioterapi, trening og ergoterapi

Tab. 4: Systematiske oversikter om effekten av fysioterapi, trening og/eller ergoterapi

	Referanse	Sammendrag
1.	Plowman EK. **Is There a Role for Exercise in the Management of Bulbar Dysfunction in Amyotrophic Lateral Sclerosis?** Journal of Speech Language & Hearing Research 2015;58(4):1151-1166.	PURPOSE: The role of exercise in the management of people with amyotrophic lateral sclerosis (PALS) is controversial and currently unclear. The purpose of this review article is to review literature examining the impact of limb, respiratory, and oral motor exercise on function, disease progression, and survival in PALS and the transgenic ALS animal model. METHOD: A literature review was conducted to examine relevant studies published in peer-reviewed journals between 1960 and 2014. All studies were appraised for quality of research and were assigned a level of evidence, and treatment outcomes were classified as either positive, negative, or neutral.

		RESULTS: A total of 18 exercise-based intervention studies on limb (13), respiratory (3), or speech (2) function were identified. Of the human clinical trials, 6 were experimental and 4 were exploratory. No experimental studies were identified examining the impact of targeted exercise on speech or swallowing function. Mild to moderate intensity limb or respiratory exercise, applied early in the disease, was noted to have a beneficial impact on motor function and survival. CONCLUSION: Insufficient data exist to support or refute the role of exercise in the management of bulbar dysfunction in PALS. This represents a critical area of future investigation.
2.	Eidenberger M, Nowotny S. **Inspiratory muscle training in patients with Amyotrophic Lateral Sclerosis: A systematic review**. Neurorehabilitation 2014;35(3):349-361.	BACKGROUND: Amyotrophic Lateral Sclerosis is a neurodegenerative disease with rapid involvement of the inspiratory muscles, leading to respiratory insufficiency. Death often occurs by aspiration and pneumonia. Endurance- and strength therapy within ALS are discussed controversially. OBJECTIVE: To review the current literature to assess the efficacy of inspiratory muscle training for ALS. METHOD: Systematic review, using databases as PubMed, PEDro, Cochrane and Google Scholar. INTERVENTION: Inspiratory muscle training vs. sham training or inspiratory muscle training alone. OUTCOME MEASURES: Inspiratory muscle strength, dyspnoea, quality of life and survival time. RESULTS: Four studies could be included in this review, two RCT's, one pre-experimental study and one with a historical control group. In total 73 patients underwent inspiratory muscle training. CONCLUSION: Studies varied in onset of the training, the training protocol and the outcomes measured. At time, there is limited evidence that inspiratory muscle training leads to strengthening of inspiratory muscles in ALS. Improvements made were minor, in only a few parameters and also in control groups. Survival time was significantly longer in the experimental group in one study. Interesting suppositions (diaphragm training vs. other IM training, improvement of chest wall and lung compliance) need to be examined in robustly designed future trials, defining exact therapeutic windows and interventions.
3.	Arbesman M, Sheard K. **Systematic review of the effectiveness of occupational therapy-related interventions for people with amyotrophic lateral sclerosis**. American Journal of Occupational Therapy 2014;68(1):20-26.	We describe the results of a systematic review of the literature on occupational therapy-related interventions for people with amyotrophic lateral sclerosis (ALS). The review included 14 studies. We found limited to moderate evidence that people involved in multidisciplinary programs have longer survival than those in general care and limited evidence that those in multidisciplinary programs have a higher percentage of appropriate assistive devices and higher quality of life in social functioning and mental health. Limited evidence indicates that people with ALS are satisfied with the comfort and ease of use of their power wheelchairs (PWCs). In addition, limited evidence is available that PWCs allow people to have increased interaction in the community. Evidence also is limited that some assistive devices are more helpful than others. Moderate evidence indicates that a home exercise program of daily stretching and resistance exercise results in improved function. The implications for practice, education, and research are discussed. Copyright © 2014 by the American Occupational Therapy Association, Inc.

4.	Arbesman M, Lieberman D, Berlanstein DR. **Method for the systematic reviews on occupational therapy and neurodegenerative diseases**. American Journal of Occupational Therapy 2014;68(1):15-19.	Systematic reviews of the literature relevant to neurodegenerative diseases, including Parkinson's disease (PD), multiple sclerosis (MS), and amyotrophic lateral sclerosis (ALS), are important to the practice of occupational therapy. We describe the four questions that served as the focus for systematic reviews of the effectiveness of occupational therapy interventions for PD, MS, and ALS. We include the background for the reviews; the process followed for addressing each question, including search terms and search strategy; the databases searched; and the methods used to summarize and critically appraise the literature. The final number of articles included in each systematic review; a summary of the themes of the results; the strengths and limitations of the findings; and implications for practice, education, and research are presented. Copyright © 2014 by the American Occupational Therapy Association, Inc.
5.	Versterre S, Buus L. **Physical therapy and exercises to patients with ALS**. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 2013;14:76.	Background: Danish physical therapists in the ALS teams are responsible for exercise guidance, evaluating needs for assistive devices, and chest physical therapy. Until now there has been no consensus among physical therapists, in Denmark, about which treatment to use and when to use it. Only very few articles, describe in detail the treatment given by physical therapist to patients with ALS. Objectives: The aim of this study was to investigate which treatment is used, what is the evidence for the treatment, what treatment/instructions do the patient think is important, and based on that create a national clinical guideline in Denmark. Methods: Fourteen hospitals in Denmark diagnose and treat patients with ALS. Thirteen have an ALS team, with a physical therapist. All 13 teams are included in the study. The study is divided into three steps. Step 1: Involvement of the physical therapists: (a) Answering a semistructured questionaire about their treatment strategies to patients with ALS; (b) Participation in a workshop, with focus on discussion of evidence, treatment strategies and creating consensus about the physiotherapeutic treatment to patients with ALS in the hospitals in Denmark; and (c) Qualifying the clinical guideline by testing it in clinical practice. Step 2: Involvement of the literature: (a) A systematic search in the databases Pubmed, Cinahl, Cochrane and Pedro and (b) Evidence extracted. Step 3: Involvement of the patients: (a) A focus group interview to assess what the patients think is important in the physical therapy treatment/instruction and (b) The clinical guideline is sent in consultation. In the process there has been contact to The Danish Institute for Clinical Guidelines. Results: Both the physical therapists, the patients and the literature agree that the physical therapist has an important role in guidance regarding respiration, exercise and assistive devices. Five papers included data about exercise and 12 about chest physical therapy. A national clinical guideline has been made and contains nine recommendations on exercise and 12 on chest physical therapy based on evidence level B - D. Discussion and conclusion: A clinical guideline has been made and builds on best practice experience from the Danish ALS physical therapist, the patient view and evidence from the literature. The evidence level is low because there is lack of resource regarding exercise and chest physical therapy to patients with ALS, and there is a high dropout rate in the studies due to the nature of the disease. By standardizing physical therapy to ALS patients in Denmark, treatment quality is ensured and resources are made possible.

6.	Reyes A, Ziman M, Nosaka K. **Respiratory muscle training for respiratory deficits in neurodegenerative disorders: a systematic review**. Chest 2013;143(5):1386-1394.	BACKGROUND: Studies of the impact of respiratory muscle training (RMT) on central neurodegenerative pathologies have been aimed at improving pulmonary function. However, there is no certainty about the effectiveness of RMT in patients affected by these groups of disorders. The purpose of this review was to assess the evidence regarding the efficacy of inspiratory muscle training (IMT) and expiratory muscle training (EMT) on respiratory function in patients with neurodegenerative disorders of the CNS. METHODS: A comprehensive search from 1990 to September 2012 on MEDLINE, Physiotherapy Evidence Database (PEDro), PubMed, Cochrane Library, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases was made. Studies reporting on IMT and EMT in patients with neurodegenerative diseases were included. The selected studies were abstracted using a standardized data collection instrument and were assessed by a quality checklist created and adapted from CONSORT (Consolidated Standards for Reporting Trials) and TREND (Transparent Reporting of Evaluation with Nonrandomized Designs). RESULTS: Twenty-four studies were identified by the search strategy. Only 19 studies met the criteria for full review. Ten studies met all the inclusion criteria and were included in the final analysis. Of the 16 parameters present in the quality assessment checklist, only six were achieved for the studies analyzed. CONCLUSIONS: There is some evidence that RMT improves a number of respiratory function parameters in patients with Parkinson disease and multiple sclerosis; however, the number of studies and their quality are not sufficient to conclude whether IMT or EMT is effective in improving respiratory function in patients with neurodegenerative disorders of the CNS.
7.	Offeringa A, Broek Ten J, Oudenaarden J, Schaaf Van Der M. **Multidisciplinary allied health practice guidelines for physical, speech and occupational therapy in ALS**. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 2013;14:64.	Background: Evidence-based clinical practice guidelines improve quality, effectiveness and appropriateness of patient care. For ALS, such guidelines are not available for the allied health care professions. Objectives: The aim of this project was to systematically develop guidelines for the multidisciplinary rehabilitation management of patients with ALS. The recommendations will support physical, speech and occupational therapists in clinical decision making with respect to the diagnosis, treatment and evaluation of relevant impairments and restrictions in functioning, activities and participation of patients with ALS. Methods: A taskforce was formed and they started the project. The International Classification of Functioning, Disability and Health (1) formed the base. The guidelines were developed according to the model from the Dutch Institute for Healthcare Improvement (CBO) 'Evidence based guideline development' (2). This model contains the following steps: systematic literature search, quality assessment and summary of the evidence; formulation of concept recommendations; feedback from experts; rephrase of recommendations; final approval and authorisation by relevant stakeholders. Results: The project resulted in practice guidelines with recommendations regarding diagnostics, intervention and evaluation of functioning within the relevant domains of the International Classification of Functioning, Disability and Health (1). The recommendations were developed for physical, speech and occupational therapists concerning all rehabilitation stages integrating evidence from research and clinical expertise of expert health care professionals, patients and their carer's preferences, national associations of physical therapy, speech therapy and occupational therapy and of the Netherlands ALS Center. In addition to the practice guidelines and the recommendations, a summary of the clinical reasoning process in algorithms is provided. The guidelines are e-published in Dutch and available at www.

		als-centrum.nl/als-richtlijn/ with free downloads. Discussion and conclusion: The development of the multidisciplinary guidelines has allowed recommendations on diagnostic and therapeutic interventions for physical, speech and occupational therapists working with patients with ALS. Implementation of the guidelines will improve standardization and transparency of the diagnostic and therapeutic process. As the guidelines were developed simultaneously for these three allied health care professions, interdisciplinary aspects of treatment are covered as well which will improve care and quality of life for patients with ALS. Implementation of these guidelines is the next crucial step to take.
8.	Dal Bello-Haas V, Florence JM. **Therapeutic exercise for people with amyotrophic lateral sclerosis or motor neuron disease**. Cochrane Database of Systematic Reviews 2013;(5)CD005229.	BACKGROUND: Despite the high incidence of muscle weakness in individuals with amyotrophic lateral sclerosis (ALS) or motor neuron disease (MND), the effects of exercise in this population are not well understood. This is an update of a review first published in 2008. OBJECTIVES: To systematically review randomised and quasi-randomised studies of exercise for people with ALS or MND. SEARCH METHODS: We searched The Cochrane Neuromuscular Disease Group Specialized Register (2 July 2012), CENTRAL (2012, Issue 6 in The Cochrane Library), MEDLINE (January 1966 to June 2012), EMBASE (January 1980 to June 2012), AMED (January 1985 to June 2012), CINAHL Plus (January 1938 to June 2012), LILACS (January 1982 to June 2012), Ovid HealthSTAR (January 1975 to December 2012). We also searched ProQuest Dissertations & Theses A&I (2007 to 2012), inspected the reference lists of all papers selected for review and contacted authors with expertise in the field. SELECTION CRITERIA: We included randomised or quasi-randomised controlled trials of people with a diagnosis of definite, probable, probable with laboratory support, or possible ALS, as defined by the El Escorial criteria. We included progressive resistance or strengthening exercise, and endurance or aerobic exercise. The control condition was no exercise or standard rehabilitation management. Our primary outcome measure was improvement in functional ability, decrease in disability or reduction in rate of decline as measured by a validated outcome tool at three months. Our secondary outcome measures were improvement in psychological status or quality of life, decrease in fatigue, increase in, or reduction in rate of decline of muscle strength (strengthening or resistance studies), increase in, or reduction in rate of decline of aerobic endurance (aerobic or endurance studies) at three months and frequency of adverse effects. We did not exclude studies on the basis of measurement of outcomes. DATA COLLECTION AND ANALYSIS: Two review authors independently assessed trial quality and extracted the data. We collected adverse event data from included trials. The review authors contacted the authors of the included studies to obtain information not available in the published articles. MAIN RESULTS: We identified two randomised controlled trials that met our inclusion criteria, and we found no new trials when we updated the searches in 2012. The first, a study with overall unclear risk of bias, examined the effects of a twice-daily exercise program of moderate load endurance exercise versus "usual activities" in 25 people with ALS. The second, a study with overall low risk of bias, examined the effects of thrice weekly moderate load and moderate intensity resistance exercises compared to usual care (stretching exercises) in 27 people with ALS. After three months, when the results of the two trials were combined (43 participants), there was a significant mean improvement in the Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS) measure of function in favour of the exercise groups (mean difference 3.21, 95% confidence interval 0.46 to 5.96). No statistically

		significant differences in quality of life, fatigue or muscle strength were found. In both trials adverse effects, investigators reported no adverse effects such as increased muscle cramping, muscle soreness or fatigue. AUTHORS' CONCLUSIONS: The included studies were too small to determine to what extent strengthening exercises for people with ALS are beneficial, or whether exercise is harmful. There is a complete lack of randomised or quasi-randomised clinical trials examining aerobic exercise in this population. More research is needed.
9.	Versterre S. **Physiotherapy and exercise to patients with amyotrophic lateral sclerosis (ALS)**. Amyotrophic Lateral Sclerosis 2012;13:145-146.	Background: Physiotherapists in Denmark have an important role in guidance regarding respiration, exercise and assistive devices to patients with amyotrophic lateral sclerosis (ALS). There is no current consensus among physiotherapists in Denmark about which treatments to use and when to use them. In the literature very few papers describe treatment given by physiotherapists to patients with ALS. The aim of this study is to investigate which treatments are used, the evidence for these treatments and whether it is possible to create consensus on a clinical guideline in Denmark built on clinical experience and evidence. The study started on 1 January 2012 with expected completion in December 2012. Objectives: 13 hospitals in Denmark diagnose and treat patients with ALS. They all have an ALS-team with at least one physiotherapist. All 13 teams are included in this study. The populations in the area of the 13 hospitals are comparable. Methods: The study consists of three steps: Step one: 16 team-physiotherapists have received and answered a semi-structured questionnaire about their treatment strategies for patients with ALS. Step two: A systematic search for literature in the databases Medline, Cinahl, Cochrane and Pedro was made. Publications of evidence level Ia and Ib were read systematically and critically. Step three: All team-physiotherapists were invited to a workshop with focus on discussion of evidence and treatment strategies. Results: The aim of this study is to reach consensus about the physiotherapy treatments for patients with ALS in the hospitals in Denmark and to publish a national clinical guideline. Step one: 16 out of 19 physiotherapists answered the questionnaire. All physiotherapists give instructions to patients in exercises and respiratory aid and support, but the instructions were different in each of the 13 hospitals. Step two: 7 papers about exercises and 14 papers about respiratory support and exercise were included for critical reading. There was good evidence for non-invasive ventilation (NIV) but no guidelines for exercises were found. Step three: 12 hospitals were represented by physiotherapists at the workshop. Agreement was reached on a clinical guideline. Knowledge from clinical practice and evidence from the literature will result in a national clinical guideline. The guideline will include optimal time for respiratory aid and support, guidance on respiratory support, training instructions and cough-support. Discussion and conclusion: We have found good clinical practice points for training in our literature study but no strong evidence. Several studies recommend NIV as a respiratory support also in the early stage of ALS. In the future, physiotherapists in Denmark will focus on earlier use of NIV, regular tests of lung function and recommendations on exercise.

10. Ivy C. **Upper extremity orthoses in ALS/MND**. Amyotrophic Lateral Sclerosis 2012;13:149-150.	Background: Occupational Therapists often provide custom and pre fabricated Orthoses for support and bracing of weak and ineffective joints or muscles of the upper extremity in the management of ALS/MND. The purpose of the orthosis is to decrease the effects of muscle imbalance to provide greater ease in performance of activities of daily living (ADLs), prevent joint contracture, and to relieve pain. Objectives: The objective of this study is to perform a systematic review of the literature as well as to draw on experiences in the ALS clinic to determine which upper extremity orthotic devices are useful for pts with ALS/MND. Methods: A systematic review of the literature available on Medline, EMBASE, Google Scholar, PubMed, and Cinahl was performed; 32 articles were appraised by one author according to a standard format. Observational, qualitative, and quantitative studies were included. In addition, the author drew on her own experience over the past 25 years with ALS/ MND patients. Results: No randomized controlled trials or controlled clinical trials were identified. A summary of descriptive and qualitative studies that relate to upper extremity orthoses as well as results in the author's experience will be discussed. Discussion and conclusions: Although there were no randomized controlled trials, five upper extremity orthoses are discussed. These will be described with photographs and case descriptions in this poster. The orthoses can be categorized as volar and dorsal wrist, proximal interphalangeal (PIP) finger extension, night resting, thumb opposition, and orthoses designed for a specific function. Further research is needed into appropriate study designs for the use of upper extremity orthoses and the best manner of assessing outcomes with this intervention. Case experience (Level 5 Evidence: "Expert Opinion") reveals functional advantage to use of the above stated orthoses.
11. Orsini M, de Freitas MRG, Mello MP, Antonioli RdS, Reis JPB, Nascimento OJM, et al. **Physical rehabilitation in amyotrophic lateral sclerosis. [Portuguese]**. Revista Neurociencias 2009;17(1):30-36.	Objective. To attempt the engaged professionals of health with the physical rehabilitation, about the existing risks in the treatment of patients with amyotrophic lateral sclerosis (ALS) in what concerns to the extreme use or the atrophy for disuse. Method. They were researched the articles in the period of 1958 to 2006 located in the databases Bireme, SciELO, Pubmed, Lilacs, by means of the following keywords: amyotrophic lateral sclerosis, Neuromuscular disease, fatigue, muscular weakness, physical activity, rehabilitation, physiotherapy. Results. The treatment of ALS aims at the prevention of the fatigue and the damages by excessive use, besides optimizing independence and of the functional capacity, through moderate exercises, stretching, adaptive equipments and physiotherapy respiratory. Conclusion. Although they have not many intervention studies involving exercises for improve strength in individuals with ALS due to the course variable and the bulbar involvement, the physical therapist, upon proposing programs with such purpose, should utilize exercises in submaximal levels in the hope attenuate the loss of force, considering the prevention of the excessive use and of the atrophy for disuse and attempting always for the adequate management.
12. Lui AJ, Byl NN. **A systematic review of the effect of moderate intensity exercise on**	BACKGROUND AND PURPOSE: Amyotrophic lateral sclerosis (ALS) is an idiopathic disease of adults affecting upper and lower motor neurons. In one to four years, progressive weakness, spasticity, and respiratory insufficiency compromise independence and survival. Current medical treatment is limited to medication and supportive care. The benefit and harm of moderate physical

	function and disease progression in amyotrophic lateral sclerosis. Journal of Neurologic Physical Therapy 2009;33(2):68-87.	exercise are controversial. This review examined current research related to moderate exercise for maintaining independence without accelerating disease progression in persons with ALS. METHODS: An evidence-based search was conducted using keywords alone and in combination (ALS, exercise, Lou Gehrig's disease, physical therapy) to search PubMed, PEDro, Hooked on Evidence, Ovid, and Cochrane databases. Human and animal models were included and graded on level of evidence and strength of recommendations for developing guidelines to practice. A secondary reviewer evaluated all selected studies, and statistics were calculated. RESULTS: The search yielded the following nine studies: four small clinical studies, one clinical systematic review, and four randomized, controlled trials based on animal models. In human studies, there were small to moderate effect sizes supporting the benefit of moderate exercise in persons with early-stage ALS, with no adverse affects on disease progression or survival time. In transgenic mice with superoxide dismutase-1 ALS, moderate exercise most often had a moderate effect size for increasing life span. DISCUSSION AND CONCLUSION: Large randomized clinical trials are needed to develop specific exercise guidelines. However, evidence suggests that moderate exercise is not associated with adverse outcomes in persons with early-stage ALS. Moderate exercise programs can be safely adapted to abilities, interests, specific response to exercise, accessibility, and family support.
13.	Campos TSP, Favero FM. **Aquatic and floor exercises for Amyotrophic Lateral Sclerosis patients: Literature review. [Portuguese]**. Revista Neurociencias 2009;17(2):170-177.	Introduction. Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease that attacks the motor neurons in the brain and in the spinal cord. The ALS patient loses the ability to accomplish the muscular contraction, originating the muscular weakness as the first symptom. Objective. Verify the effects of exercise, in both floor and water, in ALS patients. Method. A literature review was performed including the articles on exercises accomplished in floor or in water, every study design, with humans and with ALS, without year restriction. Results. Five articles were included and they demonstrated that the exercises have positive effects for patients with ALS, when supplied in a moderate way, without leading to fatigue. Conclusion. The exercises for ALS patients are very important, although the limitation in the size of the samples does not guarantee in a conclusive way that the application of any one of those exercises in other patients with ALS will have the same result. There is a little scientific evidence in the literature on the physiotherapy for ALS. Studies with larger samples are necessary for confirmation of these results.
14.	Cup EH, Pieterse AJ, Ten Broek-Pastoor JM, Munneke M, van Engelen BG, Hendricks HT, et al. **Exercise therapy and other types of physical therapy for patients with neuromuscular diseases: a**	OBJECTIVE: To summarize and critically appraise the available evidence on exercise therapy and other types of physical therapies for patients with neuromuscular diseases (NMD). DATA SOURCES: Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews, Medline, CINAHL, EMBASE (Rehabilitation and Physical Medicine), and reference lists of reviews and articles. STUDY SELECTION: Randomized clinical trials (RCTs), controlled clinical trials (CCTs), and other designs were included. Study participants had to have any of the following types of NMD: motoneuron diseases, disorders of the motor nerve roots or peripheral nerves, neuromuscular transmission disorders, or muscle diseases. All types of exercise therapy and other physical therapy

	systematic review. Archives of Physical Medicine & Rehabilitation 2007;88(11):1452-1464.	modalities were included. Outcome measures had to be at the level of body functions, activities, or participation according to the definitions of the International Classification of Functioning, Disability and Health (ICF). DATA EXTRACTION: Two reviewers independently decided on inclusion or exclusion of articles and rated the methodologic quality of the studies included. All RCTs, CCTs, and other designs only if of sufficient methodologic quality were included in a best evidence synthesis. A level of evidence was attributed for each subgroup of NMD and each type of intervention. DATA SYNTHESIS: Initially 58 studies were included: 12 RCTs, 5 CCTs, and 41 other designs. After methodologic assessment, 19 other designs were excluded from further analysis. There is level II evidence ("likely to be effective") for strengthening exercises in combination with aerobic exercises for patients with muscle disorders. Level III evidence ("indications of effectiveness") was found for aerobic exercises in patients with muscle disorders and for the combination of muscle strengthening and aerobic exercises in a heterogeneous group of muscle disorders. Finally, there is level III evidence for breathing exercises for patients with myasthenia gravis and for patients with myotonic muscular dystrophy. Adverse effects of exercise therapy were negligible. CONCLUSIONS: The available evidence is limited, but relevant for clinicians. Future studies should be preferably multicentered, and use an international classification of the variables of exercise therapy and an ICF core set for NMD in order to improve comparability of results.
15.	Morris ME, Perry A, Bilney B, Curran A, Dodd K, Wittwer JE, et al. **Outcomes of physical therapy, speech pathology, and occupational therapy for people with motor neuron disease: a systematic review**. Neurorehabilitation & Neural Repair 2006;20(3):424-434.	This article describes a systematic review and critical evaluation of the international literature on the effects of physical therapy, speech pathology, and occupational therapy for people with motor neuron disease (PwMND). The results were interpreted using the framework of the International Classification of Functioning, Disability and Health. This enabled us to summarize therapy outcomes at the level of body structure and function, activity limitations, participation restrictions, and quality of life. Databases searched included MEDLINE, PUBMED, CINAHL, PSYCInfo, Data base of Abstracts of Reviews of Effectiveness (DARE), The Physiotherapy Evidence data base (PEDro), Evidence Based Medicine Reviews (EMBASE), the Cochrane database of systematic reviews, and the Cochrane Controlled Trials Register. Evidence was graded according to the Harbour and Miller classification. Most of the evidence was found to be at the level of "clinical opinion" rather than of controlled clinical trials. Several nonrandomized small group and "observational studies" provided low-level evidence to support physical therapy for improving muscle strength and pulmonary function. There was also some evidence to support the effectiveness of speech pathology interventions for dysarthria. The search identified a small number of studies on occupational therapy for PwMND, which were small, noncontrolled pre-post-designs or clinical reports.

Kommunikasjonsteknikk

Tab. 5: Systematisk oversikt om effekten av ulike kommunikasjonsteknikker

	Referanse	Sammendrag
1.	Reigada C, Mendes O, Paiva C, Tavares M, Goncalves E. **ALS patients in locked-in syndrome: A systematic review of the literature.** Palliative Medicine 2014;28 (6):688-689.	Aim: To analyze the strategies used to communicate with amyotrophic lateral sclerosis (ALS) patients in locked-in syndrome (LIS), the decision-making process used for therapeutic interventions and the holistic process of care in general. Method: Complying the research question "how to communicate and deal with ALS patients in locked-in syndrome", we conducted a systematic review of the literature published in English using the PubMed and Scopus databases. The research keywords were (amyotrophic lateral sclerosis) [Title/Abstract] OR (motor neuron disease) [Title/Abstract] AND Locked-in [Title/Abstract]. The inclusion criteria were: scientific periodicals articles; unlimited years; age >18 years; written in English. All articles were selected and analyzed by three independent groups of reviewers. Results: Ninety one articles were identified, 17 of which fulfilled the review criteria (94% concordance between reviewers). Most of them were experimental and the number of ALS patients included varied between 1 and 21. All of the considered articles deal with the field of communication by exploring alternative communication techniques; three reported issues about the decision-making process and four described team interventions. Conclusion: The literature published is focused predominantly in alternative communication systems, all experimental, with few critically examining the holistic care needed to deal with ALS patients in LIS. In the meantime the palliative care teams are challenged to look after these patients with intense suffering and difficult ethical issues, particularly with regards to the meaning of life and medical decisions.

Kramper og spastisitet

Tab. 6: Systematiske oversikter om effekten av ulike tiltak mot kramper og spastisitet

	Referanse	Sammendrag
1.	Baldinger R, Katzberg HD, Weber M. **Treatment for cramps in amyotrophic**	BACKGROUND: Cramps are painful, involuntary muscle contractions. They commonly affect people with amyotrophic lateral sclerosis/motor neuron disease (ALS/MND) at all stages of the disease. To date, the treatment of muscle cramps in ALS has been largely empirical without any evidence from randomised controlled trials.

	lateral sclerosis/motor neuron disease. Cochrane Database of Systematic Reviews 2012;4:CD004157.	OBJECTIVES: To systematically assess the effect of interventions on muscle cramps as a primary or secondary endpoint or adverse event in people with ALS/MND. SEARCH METHODS: We searched the Cochrane Neuromuscular Disease Group Specialized Register (14 February 2011), the Cochrane Central Register of Controlled Trials (Issue 1, 2011 in The Cochrane Library), MEDLINE (January 1966 to January 2011) and EMBASE (January 1980 to January 2011) and reference lists of articles searched using the terms motor neuron disease, motor neurone disease, motoneuron disease or amyotrophic lateral sclerosis. We contacted authors of trials for further information. SELECTION CRITERIA: We included all randomised and quasi-randomised trials of oral medications in people with ALS which assessed cramps as a primary or secondary outcome measure or as an adverse event. We also included trials using subcutaneous or intravenous medications or physical therapy. DATA COLLECTION AND ANALYSIS: All authors applied the selection criteria and assessed study quality independently, and all authors performed independent data extraction. MAIN RESULTS: Twenty studies including 4789 participants were identified. Only one trial, of tetrahydrocannabinol (THC), assessed cramps as the primary endpoint. Thirteen studies assessed cramps as a secondary endpoint. The medications comprised vitamin E, baclofen, riluzole, L-threonine, xaliproden, indinavir, and memantine. Six studies assessed cramps as an adverse event. The medications comprised creatine, gabapentin, dextromethorphan, quinidine, and lithium. In all 20 studies no favourable effect for the treatment of cramps in ALS/MND could be demonstrated, but many studies were underpowered to draw a definite conclusion. A meta-analysis of two small studies showed a statistically nonsignificant result for the amino acid L-threonine for the treatment of cramps in ALS/MND. No study was identified using physical therapy as a therapeutic intervention for cramps. AUTHORS' CONCLUSIONS: There is no evidence to support the use of any intervention for muscle cramps in ALS/MND. More and larger randomised controlled trials evaluating treatments for muscle cramps in ALS/MND are needed.
2.	Ashworth NL, Satkunam LE, Deforge D. **Treatment for spasticity in amyotrophic lateral sclerosis/motor neuron disease**. Cochrane Database of	BACKGROUND: Spasticity commonly affects patients with motor neuron disease. It is likely to contribute to worsening muscle dysfunction, increased difficulty with activities of daily living and deteriorating quality of life. This is an update of a review first published in 2003 and previously updated in 2005 and 2008. OBJECTIVES: The objective of this review is to systematically review treatments for spasticity in amyotrophic lateral sclerosis, also known as motor neuron disease. SEARCH METHODS: We searched the Cochrane Neuromuscular Disease Group Specialized Register (4 July 2011), CENTRAL (2011, Issue 2), MEDLINE (January 1966 to July 2011), EMBASE (January 1980 to July 2011), CINAHL

	Systematic Reviews 2012;2:CD004156.	Plus (January 1937 to July 2011), AMED (January 1985 to July 2011) and LILACS (January 1982 to July 2011). We reviewed the bibliographies of the randomized controlled trials identified, and contacted authors and experts in the field. SELECTION CRITERIA: We included quasi-randomized or randomized controlled trials of participants with probable or definite amyotrophic lateral sclerosis according to the El Escorial diagnostic criteria (or a revised version) or the Airlie House revision. We would have included trials of physical therapy, modalities, prescription medications, non-prescription medications, chemical neurolysis, surgical interventions, and alternative therapies. Our primary outcome measure was reduction in spasticity at three months or greater as measured by the Ashworth (or modified Ashworth) spasticity scale. Our secondary outcome measures were: validated measures based on history, physical examination, physiological measures, measures of function, measures of quality of life, all adverse events, and measures of cost. DATA COLLECTION AND ANALYSIS: Two authors independently screened the abstracts of potential trials retrieved from the searches. Two authors extracted the data. We also contacted the author of the paper and obtained information not available in the published article. All three authors assessed the methodological quality of all included trials independently. MAIN RESULTS: We identified only one randomized controlled trial that met our inclusion criteria and no further trials were identified in subsequent updates. The included study was a trial of moderate intensity, endurance type exercise versus 'usual activities' in 25 patients with amyotrophic lateral sclerosis. The risk of bias was high and no adverse events were reported. At three months patients performing the 15 minute twice daily exercises had significantly less spasticity overall (mean reduction of -0.43, 95% confidence interval (CI) -1.03 to +0.17 in the treatment group versus an increase of +0.25, 95% CI -0.46 to +0.96 in control) but the mean change between groups was not significant (-0.68, 95% CI -1.62 to +0.26), as measured by the Ashworth scale (possible scores 0 to 5, where higher is worse). AUTHORS' CONCLUSIONS: The single trial performed was too small to determine whether individualized moderate intensity endurance type exercises for the trunk and limbs are beneficial or harmful. No other medical, surgical or alternative treatment and therapy has been evaluated in a randomized fashion in this patient population. More research is needed.

Legemidler

Tab. 7: Systematiske oversikter om effekten av ulike legemidler

	Referanse	Sammendrag
1.	Belendiuk KA, Baldini LL, Bonn-Miller MO. **Narrative review of the safety and efficacy of marijuana for the treatment of commonly state-approved medical and psychiatric disorders**. Addiction Science & Clinical Practice 2015;10:10.	The present investigation aimed to provide an objective narrative review of the existing literature pertaining to the benefits and harms of marijuana use for the treatment of the most common medical and psychological conditions for which it has been allowed at the state level. Common medical conditions for which marijuana is allowed (i.e., those conditions shared by at least 80 percent of medical marijuana states) were identified as: Alzheimer's disease, amyotrophic lateral sclerosis, cachexia/wasting syndrome, cancer, Crohn's disease, epilepsy and seizures, glaucoma, hepatitis C virus, human immunodeficiency virus/acquired immunodeficiency syndrome, multiple sclerosis and muscle spasticity, severe and chronic pain, and severe nausea. Post-traumatic stress disorder was also included in the review, as it is the sole psychological disorder for which medical marijuana has been allowed. Studies for this narrative review were included based on a literature search in PsycINFO, MEDLINE, and Google Scholar. Findings indicate that, for the majority of these conditions, there is insufficient evidence to support the recommendation of medical marijuana at this time. A significant amount of rigorous research is needed to definitively ascertain the potential implications of marijuana for these conditions. It is important for such work to not only examine the effects of smoked marijuana preparations, but also to compare its safety, tolerability, and efficacy in relation to existing pharmacological treatments.
2.	Deepmala, Slattery J, Kumar N, Delhey L, Berk M, Dean O, et al. **Clinical trials of N-acetylcysteine in psychiatry and neurology: A systematic review**. Neuroscience and Biobehavioral Reviews 2015;55:294-321.	N-acetylcysteine (NAC) is recognized for its role in acetaminophen overdose and as a mucolytic. Over the past decade, there has been growing evidence for the use of NAC in treating psychiatric and neurological disorders, considering its role in attenuating pathophysiological processes associated with these disorders, including oxidative stress, apoptosis, mitochondrial dysfunction, neuroinflammation and glutamate and dopamine dysregulation. In this systematic review we find favorable evidence for the use of NAC in several psychiatric and neurological disorders, particularly autism, Alzheimer's disease, cocaine and cannabis addiction, bipolar disorder, depression, trichotillomania, nail biting, skin picking, obsessive-com-

		pulsive disorder, schizophrenia, drug-induced neuropathy and progressive myoclonic epilepsy. Disorders such as anxiety, attention deficit hyperactivity disorder and mild traumatic brain injury have preliminary evidence and require larger confirmatory studies while current evidence does not support the use of NAC in gambling, methamphetamine and nicotine addictions and amyotrophic lateral sclerosis. Overall, NAC treatment appears to be safe and tolerable. Further well designed, larger controlled trials are needed for specific psychiatric and neurological disorders where the evidence is favorable.
3.	Squires N, Humberstone M, Wills A, Arthur A. **The use of botulinum toxin injections to manage drooling in amyotrophic lateral sclerosis/motor neurone disease: a systematic review**. Dysphagia 2014;29(4):500-508.	Abstract: Difficulty in managing oral secretions is commonly experienced by patients with amyotrophic lateral sclerosis (ALS)/motor neurone disease (MND) and associated bulbar weakness including dysphagia. There are no definitive evidence-based treatment guidelines to manage the distressing symptom of drooling. We reviewed the evidence for the effectiveness of botulinum toxin injections to reduce saliva in ALS/MND. The search strategy was conducted in four stages: (1) electronic search of relevant databases, (2) hand searches of all international ALS/MND symposium journals, (3) email request to MND care centres in the UK and Ireland, and (4) hand searching of reference lists. All studies were critically appraised and relevant data extracted. Botulinum toxin type A and type B were analysed separately. Due to heterogeneity, it was not possible to calculate a pooled estimate of effect. Twelve studies met the inclusion criteria (9 for type A and 3 for type B). Only two randomised controlled trials were identified. Study sample sizes were small with a mean of 12.5 subjects. The most frequently reported outcomes were weight of cotton rolls and number of tissues used. All studies claimed the intervention tested was effective, but only seven studies (4 for type A and 3 for type B) reported statistically significant differences. Although there is evidence to suggest that botulinum toxin B can reduce drooling, the evidence base is limited by a lack of randomized controlled trials. Evidence to support the use of botulinum toxin A is weaker. Larger trials will help remove the uncertainty practitioners face in treating this disabling symptom.
4.	**Enercel homeopathic medicine for patient with infectious diseases and motor neuron disease.** Health Technology Assessment Section, Medical Development Division, Ministry of Health, Malaysia; 2014. (Technology Review Report 001/2014).	Sammendrag ikke tilgjengelig.

5.	Zheng Z, Sheng L, Shang H. **Statins and amyotrophic lateral sclerosis: a systematic review and meta-analysis**. Amyotrophic Lateral sclerosis & Frontotemporal Degeneration 2013;14(4):241-245.	OBJECTIVE: To evaluate the association between statins and the incidence and progression of amyotrophic lateral sclerosis (ALS). METHODS: Several electronic databases (PubMed, Embase, and EBSCO) and Chinese databases (CBM, Wanfang, and VIP) were searched for original articles on April 1(st), 2012. Case-control and cohort studies that provide information on the association between statins and ALS were considered eligible for inclusion. A systematic review was conducted to evaluate the association of statins and the incidence and progression of ALS. RESULTS: Two case-control studies and one cohort study that relate the risk of ALS to statins satisfied the inclusion criteria for the meta-analysis. The pooled rate ratio of statin use was 0.89 [95% CI, 0.55 to 1.42] for ALS patients versus non-ALS patients. Three cohort studies on the association between statins and the progression of ALS were identified; these suggested that no strong evidence for the statin-ALS progression relationship exists. No cohort studies favor the use of statins on ALS patients. CONCLUSIONS: No definite association between statin use and ALS incidence and progression has been found. Existing results are currently inconclusive to make scientifically supported conclusions. Further prospective cohort studies are still needed.
6.	Stokholm MG, Bisgard C, Vilholm OJ. **Safety and administration of treatment with botulinum neurotoxin for sialorrhoea in ALS patients: review of the literature and a proposal for tailored treatment**. Amyotrophic Lateral sclerosis & Frontotemporal Degeneration 2013;14(7-8):516-520.	Botulinum neurotoxin (BoNT) is a second-line treatment of sialorrhoea in ALS (amyotrophic lateral sclerosis) patients. This article is a review of the published literature concerning safety and administration of this treatment to ALS patients. A PubMed search was performed. All original publications on BoNT treatment of sialorrhoea in ALS patients were included in the review. Only a few adverse events were observed concerning treatment with BoNT. The studies performed to date have applied different treatment strategies with different dosages. In conclusion, BoNT treatment for sialorrhoea in ALS patients is safe with few adverse effects. The authors advocate for the implementation of a personalized treatment strategy. Special precautions must be taken when patients do not have the assistance of a ventilator and a feeding tube.
7.	Gamez J, Salvado M, Martinez de la Ossa A, Badia M. **Lithium for treatment of amyotrophic lateral sclerosis: much ado about nothing**. Neurologia 2013.	INTRODUCTION: Lithium was proposed in 2008 as an effective candidate in the treatment of ALS after a report claimed that it was able to delay functional deterioration by 40% and that none of the 16 patients treated with a combination of lithium plus riluzole had died during a 15-month follow-up period. The excellent results of this pilot study engendered considerable optimism among patients, their families, patients' associations, and the scientific community. This report sparked numerous phase ii clinical trials. Many patients who were not included in these studies used all resources at their disposal to access

	Apr 10. pii: S0213-4853(13)00021-2. doi: 10.1016/j.nrl.2013.02.001. [Epub ahead of print]	the drug as treatment under a compassionate use programme. OBJECTIVES: To evaluate the effectiveness of lithium in ALS using a meta-analysis of the information reported in 12 studies which were examined for methodological quality. MATERIAL AND METHODS: . Searches were performed using MEDLINE, EMBASE, the Cochrane Neuromuscular Disease Group Trials Register, ClinicalTrials.gov, and EudraCT (January 1996-August 2012). RESULTS: To date, we have information on more 1100 patients treated with lithium. Unfortunately, the results do not confirm the positive effect described in the pilot study, which suggests that this drug is not effective at slowing disease progression. Two trials had to be suspended before the scheduled completion date due to the ineffectiveness of the drug as well as numerous adverse effects. A recently published study also ruled out any possible modest effect. CONCLUSIONS: There is evidence to suggest that lithium has no short-term benefits in ALS. A comparison of the group of patients treated with lithium+riluzole and the control group treated with riluzole alone showed no statistically significant differences in rates of functional decline, deterioration of respiratory function, or survival time. Furthermore, there was no evidence that it was more effective than the placebo.
8.	Brettschneider J, Kurent J, Ludolph A. **Drug therapy for pain in amyotrophic lateral sclerosis or motor neuron disease**. Cochrane Database of Systematic Reviews 2013(6):CD005226.	BACKGROUND: Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease (MND), is the most common neurodegenerative disorder of the motor system in adults. Pain in ALS is a frequent symptom especially in the later stages of disease and can have a pronounced influence on quality of life and suffering. Treatment of pain therefore should be recognised as an important aspect of palliative care in ALS. This is an update of a review first published in 2008. OBJECTIVES: To systematically review the evidence for the efficacy of drug therapy in relieving pain in ALS. We also aimed to evaluate possible adverse effects associated with the different drugs and their influence on survival and quality of life. SEARCH METHODS: On 2 July 2012, we searched the following databases: the Cochrane Neuromuscular Disease Group Specialized Register (2 July 2012), CENTRAL (2012, Issue 6 in The Cochrane Library), MEDLINE (January 1966 to June 2012), EMBASE (January 1980 to June 2012), CINAHL (January 1982 to June 2012), AMED (January 1985 to June 2012) and LILACS (January 1982 to June 2012). We checked the bibliographies of trials identified and contacted other disease experts to identify further published and unpublished trials. SELECTION CRITERIA: We searched for randomised or quasi-randomised controlled trials on drug therapy for pain in amyotrophic lateral sclerosis. DATA COLLECTION AND ANALYSIS: We collected data using a specially designed form and analysed them using the Cochrane Review Manager software. MAIN RESULTS: We found no randomised or quasi-randomised controlled trials on drug therapy for pain in ALS or MND.

		AUTHORS' CONCLUSIONS: There is no evidence from randomised controlled trials about the management of pain in ALS. Further research on this important aspect of palliative care in ALS is needed. Randomised controlled trials should be initiated to determine the effectiveness of different analgesics for treatment of pain in ALS.
9.	Pastula DM, Moore DH, Bedlack RS. **Creatine for amyotrophic lateral sclerosis/motor neuron disease**. Cochrane Database of Systematic Reviews 2012(12):CD005225.	BACKGROUND: Creatine, a naturally-occurring nitrogenous organic acid involved in adenosine triphosphate (ATP) production, has been shown to increase survival in mouse models of amyotrophic lateral sclerosis (ALS), also known as motor neuron disease (MND). Results from human trials, however, have been mixed. Given conflicting results regarding the efficacy of creatine, we conducted a systematic review, which was updated in 2012. OBJECTIVES: To systematically examine the efficacy of creatine efficacy in prolonging ALS survival and in slowing ALS disease progression. SEARCH METHODS: We searched the Cochrane Neuromuscular Disease Group Specialized Register (16 July 2012), CENTRAL (2012, issue 7 in the Cochrane Library), MEDLINE (January 1966 to July 2012) and EMBASE (January 1980 to July 2012) for any trial involving creatine in the treatment of ALS. We also contacted experts in the field for any additional studies. SELECTION CRITERIA: Randomized trials of treatment with creatine or placebo in patients diagnosed with ALS. Our primary outcome was tracheostomy-free survival time; secondary outcomes were ALS progression as measured by changes in ALS functional rating revised scores (ALSFRS-R) and per cent predicted forced vital capacity (FVC) over time. DATA COLLECTION AND ANALYSIS: Two authors independently selected studies, assessed risk of bias and extracted data. We obtained and analyzed individual participant data from each study. MAIN RESULTS: We included three trials involving 386 participants randomized to either creatine 5 to 10 g per day or placebo. When we updated the searches in 2012 we found no additional trials. Creatine was reportedly well-tolerated in all three included studies, with no evidence of renal failure or serious adverse events specifically attributable to creatine. Using a pooled log-rank statistical test, we found no statistical difference in survival between the placebo and creatine groups across all three studies (Chi(2) = 0.09, P = 0.76). In addition, we found no statistical difference in ALSFRS-R slopes between the two groups across all three studies using a pooled linear mixed-effects model (slope difference of +0.03 ALSFRS-R/month in the creatine group; P = 0.76). Interestingly, there was a trend towards slightly worsened FVC slope in the creatine group (slope difference of -0.63 FVC/month in the creatine group) using a pooled linear mixed-effects model across the two studies which included FVC as an outcome, but this difference was not statistically significant (P = 0.054).

		AUTHORS' CONCLUSIONS: In patients already diagnosed with clinically probable or definite ALS, creatine at doses ranging from 5 to 10 g per day did not have a statistically significant effect on survival, ALSFRS-R progression or percent predicted FVC progression.
10.	Nihr HSC. **Dexpramipexole for amyotrophic lateral sclerosis**. Birmingham: NIHR Horizon Scanning Centre (NIHR HSC); 2012.	Sammendrag ikke tilgjengelig.
11.	Morren JA, Galvez-Jimenez N. **Current and prospective disease-modifying therapies for amyotrophic lateral sclerosis**. Expert Opinion on Investigational Drugs 2012;21(3):297-320.	Abstract: INTRODUCTION: Amyotrophic lateral sclerosis (ALS) is a devastating illness of unclear etiology affecting motor neurons. It causes unremitting muscle paralysis, atrophy and death usually within 3 - 5 years from diagnosis. The human and economic costs for those affected are sobering. To date, tremendous efforts have failed to find a cure. AREAS COVERED: An extensive literature search was undertaken using Medline and the Cochrane Systematic Review and Clinical Trial databases. Riluzole and investigational ALS drugs are discussed. Riluzole is the only approved disease-modifying therapy despite its modest effect on survival. Recent research has produced promising agents aimed at better disease control if not a cure. This review discusses agents targeting neuronal glutamate excitotoxicity, protein misfolding and accumulation, autophagy, apoptosis, mitochondrial dysfunction, free radical oxidative injury, immunomodulation, mutant mRNA counteraction, muscle physiology, neurotrophic factors and stem cell applications. The challenges in ALS drug development are highlighted. EXPERT OPINION: Riluzole should be used for patients with definite, probable, suspected or possible ALS by World Federation of Neurology diagnostic criteria. Systematic monitoring for hepatic dysfunction, neutropenia and other serious adverse effects should be done routinely as outlined. All ALS patients should consider genetic screening and enrollment in ALS trials guided by the data reviewed.
12.	Miller RG, Mitchell JD, Moore DH. **Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND)**. Cochrane Database of Systematic Reviews 2012(3): CD001447.	BACKGROUND: Riluzole is approved for the treatment of amyotrophic lateral sclerosis in most countries. Questions persist about its clinical utility because of high cost and modest efficacy. OBJECTIVES: To examine the efficacy of riluzole in prolonging survival and in delaying the use of surrogates (tracheostomy and mechanical ventilation) to sustain survival, and to assess the effect of riluzole upon functional health. SEARCH METHODS: We searched the Cochrane Neuromuscular Disease Group Specialized Register (20 April 2011), the Cochrane Central Register of Controlled Trials (CENTRAL)

		(2011, Issue 2), MEDLINE (1966 to April 2011), EMBASE (1980 to May 2011) and made enquiries of authors of trials, Aventis (manufacturer of riluzole) and other experts in the field. SELECTION CRITERIA: Types of studies: randomized controlled trials TYPES OF PARTICIPANTS: adults with a diagnosis of amyotrophic lateral sclerosis Types of interventions: treatment with riluzole or placebo Types of outcome measures: Primary: pooled hazard ratio of tracheostomy-free survival over all time points with riluzole 100 mg. Secondary: per cent mortality with riluzole 50 mg, 100 mg and 200 mg; neurologic function, muscle strength and adverse events. DATA COLLECTION AND ANALYSIS: One author performed data extraction and two other authors checked them. One author checked the data and entered them into the computer. The other authors verified the data entry. We obtained missing data from the trial authors whenever possible. MAIN RESULTS: The four trials examining tracheostomy-free survival included a total of 974 riluzole-treated patients and 503 placebo-treated patients. No new randomized controlled trials were found when we updated the searches for this update in 2011. The methodological quality was acceptable and three trials were easily comparable, although one trial (169 participants) included older patients in more advanced stages of amyotrophic lateral sclerosis and one (195 participants) had multiple primary endpoints. Riluzole 100 mg per day provided a benefit for the homogeneous group of patients in the first two trials (hazard ratio (HR) 0.80, 95% confidence internal (CI) 0.64 to 0.99, P= 0.042) and there was no evidence of heterogeneity (P = 0.33). When the third trial (which included older and more seriously affected patients) was added, there was evidence of heterogeneity (P < 0.0001) and the overall treatment effect was reduced but still significant (HR 0.84, 95% CI 0.698 to 0.997, P= 0.046). This represented a 9% gain in the probability of surviving one year (49% in the placebo and 58% in the riluzole group), and increased median survival from 11.8 to 14.8 months. There was a small beneficial effect on both bulbar and limb function, but not on muscle strength. A three-fold increase in serum alanine transferase was more frequent in riluzole-treated patients than controls (mean difference 2.62, 95% CI 1.59 to 4.31). AUTHORS' CONCLUSIONS: Riluzole 100 mg daily is reasonably safe and probably prolongs median survival by about two to three months in patients with amyotrophic lateral sclerosis.
13.	Michel B, Mitchell JD, John HJW, Gian Domenico B. **Recombinant human insulin-like growth factor I (rhIGF-I) for the treatment of amyotrophic lateral sclerosis/motor neuron disease**.	BACKGROUND: Recombinant human insulin-like growth factor I (rhIGF-I) is a possible disease modifying therapy for amyotrophic lateral sclerosis (ALS, which is also known as motor neuron disease (MND)). OBJECTIVES: To examine the efficacy of rhIGF-I in affecting disease progression, impact on measures of functional health status, prolonging survival and delaying the use of surrogates (tracheostomy and mechanical ventilation) to sustain survival in ALS. Occurrence of adverse events was also reviewed. SEARCH METHODS: We searched the Cochrane Neuromuscular Disease Group Specialized Register (21 November 2011), CENTRAL (2011, Issue 4), MEDLINE (January 1966 to November 2011) and EMBASE

	Cochrane Database of Systematic Reviews 2012(4):CD002064.	(January 1980 to November 2011) and sought information from the authors of randomised clinical trials and manufacturers of rhIGF-I. SELECTION CRITERIA: We considered all randomised controlled clinical trials involving rhIGF-I treatment of adults with definite or probable ALS according to the El Escorial Criteria. The primary outcome measure was change in Appel Amyotrophic Lateral Sclerosis Rating Scale (AALSRS) total score after nine months of treatment and secondary outcome measures were change in AALSRS at 1, 2, 3, 4, 5, 6, 7, 8, 9 months, change in quality of life (Sickness Impact Profile scale), survival and adverse events. DATA COLLECTION AND ANALYSIS: Each author independently graded the risk of bias in the included studies. The lead author extracted data and the other authors checked them. We generated some missing data by making ruler measurements of data in published graphs. We collected data about adverse events from the included trials. MAIN RESULTS: We identified three randomised controlled trials (RCTs) of rhIGF-I, involving 779 participants, for inclusion in the analysis. In a European trial (183 participants) the mean difference (MD) in change in AALSRS total score after nine months was -3.30 (95% confidence interval (CI) -8.68 to 2.08). In a North American trial (266 participants), the MD after nine months was -6.00 (95% CI -10.99 to -1.01). The combined analysis from both RCTs showed a MD after nine months of -4.75 (95% CI -8.41 to -1.09), a significant difference in favour of the treated group. The secondary outcome measures showed non-significant trends favouring rhIGF-I. There was an increased risk of injection site reactions with rhIGF-I (risk ratio 1.26, 95% CI 1.04 to 1.54). . A second North American trial (330 participants) used a novel primary end point involving manual muscle strength testing. No differences were demonstrated between the treated and placebo groups in this study. All three trials were at high risk of bias. AUTHORS' CONCLUSIONS: Meta-analysis revealed a significant difference in favour of rhIGF-I treatment; however, the quality of the evidence from the two included trials was low. A third study showed no difference between treatment and placebo. There is no evidence for increase in survival with IGF1. All three included trials were at high risk of bias.
14.	Benze G, Geyer A, Alt-Epping B, Nauck F. **[Treatment of nausea and vomiting with 5HT3 receptor antagonists, steroids, antihistamines, anticholinergics, somatostatinantagonists, benzodiazepines and cannabinoids in palliative care patients : a systematic review]**. Der	BACKGROUND: Various recommendations exist for the treatment of nausea and vomiting in palliative care but only few studies and even less systematic reviews look into antiemetic therapy for patients receiving palliative care. OBJECTIVES: This systematic review aims to analyze the current evidence for antiemetic treatment with 5HT3 receptor antagonists, steroids, antihistamines, anticholinergics, somatostatin analogs, benzodiazepines and cannabinoids in palliative care patients with far advanced cancer not receiving chemotherapy or radiotherapy, acquired immune deficiency syndrome (AIDS), chronic obstructive pulmonary disease (COPD), progressive heart failure, amyotrophic lateral sclerosis (ALS) or multiple sclerosis (MS). Results regarding evidence of treatment with prokinetic and neuroleptic agents will be published separately.

Schmerz 2012;26(5):481-499.	METHODS: The electronic databases PubMed and EmBase were systematically searched for studies (published 1966-2011) dealing with antiemetic therapy in palliative care and electronic retrieval was completed by manual searching. Studies with patients undergoing chemotherapy or radiotherapy, pediatric studies and studies published in languages other than English or German were excluded. Studies addressing therapy with 5HT3 receptor antagonists, steroids, antihistamines, anticholinergics, somatostatin analogs, benzodiazepines or cannabinoids were identified and selected for this systematic review. RESULTS: In the general search 75 relevant studies were found. Of those 36 addressed 5HT3 receptor antagonists, steroids, antihistamines, anticholinergics, somatostatin analogs, benzodiazepines and cannabinoids, 13 considered 5HT3 receptor antagonists, 10 somatostatin antagonists, 9 steroids, 5 cannabinoids, 4 anticholinergics, 1 antihistamines and none benzodiazepines. Furthermore six systematic reviews exist. Evidence for any drug used as an antiemetic is low. Concerning 5HT3 receptor antagonists data are insufficient for recommendations on the treatment of patients with AIDS and MS due to the small size of included patient groups. For patients with cancer contradictory results were published: the larger studies showed a positive effect of 5HT3 receptor antagonists and better efficacy, as compared to metoclopramide, dexamethasone and neuroleptics. Heterogeneous results were found for steroids, with a positive trend for patients with cancer. Data are insufficient for antihistamines. Studies prove effectiveness of butylscopolammonium in the treatment of nausea and vomiting caused by malignant gastrointestinal obstruction, whereas octreotide is superior to butylscopolammonium. Regarding benzodiazepines for symptom control of nausea and vomiting in palliative care patients no studies were detected. Cannabinoids were found to relieve nausea and vomiting in patients with cancer and AIDS but with notable side effects. Furthermore, the studies compared cannabinoids to less recent antiemetic drugs but not, for example to 5HT3 receptor antagonists. Regarding symptom control of nausea and vomiting in patients with COPD, progressive heart failure and ALS no studies were undertaken in patients receiving palliative care. CONCLUSIONS: In palliative care patients with nausea and vomiting 5HT3 receptor antagonists can be used if treatment with other antiemetics, such as metoclopramide and neuroleptics is not sufficient. There is a trend that steroids in combination with other antiemetics improve symptom relief. Cannabinoids rather have a status as a second line antiemetic. In cases of nausea and vomiting caused by malignant gastrointestinal obstruction octreotide showed the best and butylscopolammonium bromide the second best results. Concerning antihistamines and benzodiazepines insufficient data was found. Recommendations in the literature are mainly based on studies in patients with cancer. The overall strength of evidence is low. More well designed studies in palliative care patients are needed in order to provide evidence-based therapy. The English full text version of this article will be available in SpringerLink as of November 2012 (under "Supplemental").

15.	Benze G, Alt-Epping B, Geyer A, Nauck F. **[Treatment of nausea and vomiting with prokinetics and neuroleptics in palliative care patients : a review]**. Der Schmerz 2012;26(5):500-514.	BACKGROUND: Many recommendations concerning the treatment of nausea and vomiting in palliative care patients exist but what is the evidence for this? Most studies dealing with this topic have focused on cancer patients under chemotherapy and/or radiation therapy or on patients with postoperative nausea. Cancer patients without chemotherapy or radiation therapy, patients without postoperative nausea, and patients having other diseases with palliative care aspects, such as acquired immunodeficiency syndrome (AIDS), chronic obstructive pulmonary disease (COPD), progressive heart failure, amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) have been underrepresented in studies on nausea and vomiting so far. OBJECTIVES: The aim of this review was to determine the level of evidence for the treatment of nausea and vomiting with prokinetics and neuroleptics in palliative care patients suffering from far advanced cancer and no longer being treated with chemotherapy or radiation therapy, AIDS, COPD, progressive heart failure, ALS or MS. METHODS: Two different electronic databases (PubMed und Embase) were used to identify studies. Furthermore, a hand search for related articles was performed. No restriction was made concerning study types. Studies with patients undergoing chemotherapy radiation therapy or suffering from postoperative nausea, pediatric studies and studies published neither in English nor in German were excluded. RESULTS: A total of 30 studies fulfilling the inclusion criteria were found. All studies focused on cancer patients. Despite intensive research studies in patients with AIDS, COPD, heart failure, ALS or MS were not detected. Metoclopramide is seen as an effective drug in many studies whereas the evidence for it is moderate at best. Within the group of neuroleptics, levosupiride and levomepromazine seem to have good antiemetic potential but the evidence level is low. CONCLUSION: In patients with advanced cancer not being treated with chemotherapy or radiation therapy, metoclopramide can be used to reduce nausea and vomiting. Neuroleptics, such as levosulpiride or levomepromazine are alternatives but their adverse effects have to be considered carefully. The evidence level for prokinetics and neuroleptics is moderate to low. Concerning palliative care of patients with diseases other than cancer no studies exist. More well designed studies in palliative care patients are needed in order to facilitate evidence based antiemetic therapy. The English full text version of this article will be available in SpringerLink as of November 2012 (under "Supplemental").
16.	Orrell RW. **Motor neuron disease: systematic reviews of treatment for ALS**	INTRODUCTION: There is no curative treatment for the common motor neuron diseases, amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy. Nevertheless, there is an increasing volume of published studies. This review assesses the current evidence for treatment of these conditions.

	and SMA. British Medical Bulletin 2010;93:145-159.	SOURCES OF DATA: Primarily, the systematic reviews of the Cochrane Collaboration, with additional reference to other systematic reviews and online sites. AREAS OF AGREEMENT: Riluzole remains the only medication with demonstrated efficacy and regulatory approval for the treatment of ALS. AREAS OF CONTROVERSY, GROWING POINTS, AND AREAS TIMELY FOR DEVELOPING RESEARCH: The design of clinical trials and the publication of unsatisfactory studies, in both human and animal models, continue to cause confusion in advising on patient management. Improvements in trial design, critical assessment of studies for publication and avoidance of bias towards publication of positive results are needed. A better understanding of pathogenesis should lead to more potent interventions.
17.	Green AJ, De-Vries K. **Cannabis use in palliative care - an examination of the evidence and the implications for nurses**. Journal of Clinical Nursing 2010;19(17-18):2454-2462.	Abstract: AIM AND OBJECTIVE: Examine the pharmaceutical qualities of cannabis including a historical overview of cannabis use. Discuss the use of cannabis as a clinical intervention for people experiencing palliative care, including those with life-threatening chronic illness such as multiple sclerosis and motor neurone disease [amyotrophic lateral sclerosis] in the UK. BACKGROUND: The non-medicinal use of cannabis has been well documented in the media. There is a growing scientific literature on the benefits of cannabis in symptom management in cancer care. Service users, nurses and carers need to be aware of the implications for care and treatment if cannabis is being used medicinally. DESIGN: A comprehensive literature review. METHOD: Literature searches were made of databases from 1996 using the term cannabis and the combination terms of cannabis and palliative care; symptom management; cancer; oncology; chronic illness; motor neurone disease/amyotrophic lateral sclerosis; and multiple sclerosis. Internet material provided for service users searching for information about the medicinal use of cannabis was also examined. RESULTS: The literature on the use of cannabis in health care repeatedly refers to changes for users that may be equated with improvement in quality of life as an outcome of its use. This has led to increased use of cannabis by these service users. However, the cannabis used is usually obtained illegally and can have consequences for those who choose to use it for its therapeutic value and for nurses who are providing care. RELEVANCE TO CLINICAL PRACTICE: Questions and dilemmas are raised concerning the role of the nurse when caring and supporting a person making therapeutic use of cannabis.Copyright © 2010 Blackwell Publishing Ltd.

18.	Bongioanni P, Reali C, Sogos V. **Ciliary neurotrophic factor (CNTF) for amyotrophic lateral sclerosis or motor neuron disease.** Cochrane Database of Systematic Reviews 2009(4):CD004302.	Background: Amyotrophic lateral sclerosis, also known as motor neuron disease, is a fatal neuromuscular disease characterized by progressive muscle weakness resulting in paralysis. It might be treated with ciliary neurotrophic factor. This is an updated review. An updated search was performed in February 2009, but no new studies were found. Objectives: The objective of this review was to examine the efficacy of ciliary neurotrophic factor in amyotrophic lateral sclerosis. Search strategy: We updated the searches of the Cochrane Neuromuscular Disease Group Trials Register (searched to February 2009) for randomized trials, MEDLINE (from January 1966 to February 2009) and EMBASE (from January 1980 to February 2009); checked the reference lists of papers identified and contacted the authors of identified studies to get additional unpublished results. Selection criteria: We considered the following selection criteria: Types of studies: randomized controlled clinical trials. Types of participants: adults with a diagnosis of either probable or definite amyotrophic lateral sclerosis according to the El Escorial criteria. Types of interventions: treatment with ciliary neurotrophic factor for at least six months in a placebo-controlled randomized trial format. Types of outcome measures: Primary outcome: survival; Secondary outcomes: muscle strength, respiratory function, changes in bulbar functions, changes in quality of life, proportion of patients with adverse side effects (such as cough, asthenia, nausea, anorexia, weight loss and increased salivation). Data collection and analysis: We identified two randomized trials. The data were extracted and examined independently by the review authors. Some missing data were obtained from the investigators. Main results: Two trials with a total population of 1,300 amyotrophic lateral sclerosis patients who were randomized to treatment with subcutaneous injections of recombinant human ciliary neurotrophic factor or placebo were examined in this review. No new trials were found on updating the search in February 2009. The methodological quality of these trials was considered adequate. No significant difference was observed between ciliary neurotrophic factor and placebo groups for survival, the primary outcome measure. The relative risk was 1.07 (95% confidence interval (CI) 0.81 to 1.41). No significant differences between the groups were observed for most of the secondary outcomes. However, a significant increase of the incidence of several adverse events was noted in groups treated with higher doses of CNTF. Authors' conclusions: Ciliary neurotrophic factor treatment had no significant effect on amyotrophic lateral sclerosis progression. At high concentrations, several side effects were observed. A combination of ciliary neurotrophic factor with other neurotrophic factors (as suggested by results on animal models) and more efficient delivery methods should be tested. Copyright © 2009 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
19.	Tysnes OB. **Treatment of sialorrhea in amyotrophic**	BACKGROUND: Amyotrophic lateral sclerosis (ALS) is a devastating progressive disease of all voluntary muscles. Bulbar symptoms with reduced ability to swallow occur frequently and may also be an early symptom. For some patients drooling may represent a severe social problem.

	lateral sclerosis. Acta Neurologica Scandinavica Supplementum 2008;188:77-81.	AIM: To review the literature on treatment of sialorrhea in ALS and describe possible treatments. METHOD: PubMed was searched combining the words amyotrophic or ALS with sialorrhea or drooling. Publications more recent than 2000 were selected. RESULTS: A total of 31 publications were found. Of these, 22 are from 2000 or later. Thirteen of the 22 most recent publications are original papers whereas 9 are review articles. Of the original articles, four describe treatment of sialorrhea with radiotherapy, five describe effects of botolinum toxin injections into the salivary grands and two describe serious side-effects of botolinum toxin injections for sialorrhea in ALS. The remaining original articles are case descriptions or practice surveys. DISCUSSION: The treatment of sialorrhea in ALS is discussed in the view of current knowledge.
20.	Orrell RW, Lane RJ, Ross M. **A systematic review of antioxidant treatment for amyotrophic lateral sclerosis/motor neuron disease**. Amyotrophic Lateral Sclerosis 2008;9(4):195-211.	Abstract: Free radical accumulation and oxidative stress have been proposed as contributing to the progression of amyotrophic lateral sclerosis (motor neuron disease). A range of antioxidant medications is available, and has been studied. We aimed to examine the effects of antioxidant medication in the treatment of people with amyotrophic lateral sclerosis, and searched the Cochrane Neuromuscular Disease Group Trials register (August 2005), MEDLINE (January 1966 to August 2005), EMBASE (January 1980 to August 2005) and other sources. Selection criteria were all randomized or quasi-randomized controlled trials of antioxidant treatment for amyotrophic lateral sclerosis. The authors independently applied the selection criteria, assessed study quality and two authors performed independent data extraction. The search identified 23 studies for consideration but only nine studies met the inclusion criteria. Only two studies used our predetermined primary outcome measure as the primary outcome measure (survival at 12 months treatment). However, sufficient data were available from four studies to allow analysis of this outcome measure, and a meta-analysis was performed. In the individual studies no significant effect was observed for vitamin E 500 mg twice daily; vitamin E 1 g five times daily; acetylcysteine 50 mg/kg daily subcutaneous infusion; or a combination of L-methionine 2 g, vitamin E 400 International Units, and selenium 0.03 mg three times daily (Alsemet). No significant effect on the primary outcome measure was observed in a meta analysis of all antioxidants combined. No significant differences were demonstrated in any of the secondary outcome measures. In the opinion of the reviewers, there is insufficient evidence of efficacy of individual antioxidants, or antioxidants in general, in the treatment of people with amyotrophic lateral sclerosis. One study reported a mild positive effect, but this was not supported by the analysis we used. Generally, the studies were poorly designed, and underpowered, with low numbers of participants and of short duration. Further well-designed trials of medications such as vitamin C and E are unlikely to be performed. If future trials of antioxidant medications are performed, careful attention should be given to sample size, outcome measures, and duration of the trial.

		The high tolerance and safety, and relatively low cost of vitamins C and E, and other considerations related to the lack of other effective treatments for amyotrophic lateral sclerosis, explain the continuing use of these vitamins by physicians and people with amyotrophic lateral sclerosis. While there is no substantial clinical trial evidence to support their clinical use, there is no clear contraindication.
21.	Orrell RW, Lane RJM, Ross M. **Antioxidant treatment for amyotrophic lateral sclerosis / motor neuron disease**. Cochrane Database of Systematic Reviews 2007(1):CD002829.	Abstract: Background: Free radical accumulation and oxidative stress have been proposed as contributing to the progression of amyotrophic lateral sclerosis (or motor neuron disease). A range of antioxidant medications are available, and have been studied. Objectives: To examine the effects of antioxidant medication in the treatment of people with amyotrophic lateral sclerosis. Search strategy: We searched the Cochrane Neuromuscular Disease Group Trials register (August 2005), MEDLINE (from January 1966 to August 2005), EMBASE (from January 1980 to August 2005) and other sources. Selection criteria: All randomized or quasi-randomized controlled trials of antioxidant treatment for amyotrophic lateral sclerosis. Data collection and analysis: The authors independently applied the selection criteria, assessed study quality and two authors performed independent data extraction. Main results: The search identified 23 studies for consideration but only nine studies met the inclusion criteria. Only two studies used our predetermined primary outcome measure as the primary outcome measure, (survival at 12 months treatment). However, sufficient data were available from four studies to allow analysis of this outcome measure, and a meta-analysis was performed. In the individual studies no significant effect was observed for vitamin E 500 mg twice daily; vitamin E 1 g five times daily; acetylcysteine 50 mg/kg daily subcutaneous infusion; or a combination of L-methionine 2 g, vitamin E 400 International Units, and selenium 0.03mg three times daily (Alsemet). No significant effect on the primary outcome measure was observed in a meta-analysis of all antioxidants combined. No significant differences were demonstrated in any of the secondary outcome measures. Authors' conclusions: There is insufficient evidence of efficacy of individual antioxidants, or antioxidants in general, in the treatment of people with amyotrophic lateral sclerosis. One study reported a mild positive effect, but this was not supported by the analysis we used. Generally the studies were poorly designed, and underpowered, with low numbers of participants and of short duration. Further well-designed trials of medications such as vitamin C and E are unlikely to be performed. If future trials of antioxidant medications are performed, careful attention should be given to sample size, outcome measures, and duration of the trial. The high tolerance and safety, and relatively low cost of vitamins C and E, and other considerations related to the lack of other effective treatments for amyotrophic lateral sclerosis, explain the continuing use of these vitamins by physicians and people with amyotrophic lateral sclerosis. While there is no substantial clinical trial evidence to support their clinical use, there is no clear contraindication.

22.	Mitchell JD, Wokke JHJ, Borasio GD. **Recombinant human insulin-like growth factor I (rhIGF-I) for amyotrophic lateral sclerosis/motor neuron disease**. Cochrane Database of Systematic Reviews 2007(4):CD002064.	Abstract: Background: Trophic factors, including recombinant human insulin-like growth factor I (rhIGF-I) are possible disease modifying therapies for amyotrophic lateral sclerosis. Objectives: To examine the efficacy of recombinant human insulin-like growth factor I in amyotrophic lateral sclerosis. Search strategy: We searched the Cochrane Neuromuscular Disease Group Trials Register (March 2006), MEDLINE (January 1966 to March 2006) and EMBASE (January 1980 to March 2006) and asked the authors of randomised clinical trials and manufacturers of recombinant human insulin-like growth factor I. Selection criteria: We considered all randomised controlled clinical trials involving rhIGF-I treatment of amyotrophic lateral sclerosis in adults with a clinical diagnosis of definite or probable amyotrophic lateral sclerosis according to the El Escorial Criteria. The primary outcome measure was change in Appel Amyotrophic Lateral Sclerosis Rating Scale (AALSRS) total score after nine months treatment and secondary outcome measures were change in AALSRS at 1, 2, 3, 4, 5, 6, 7, 8, 9 months, change in quality of life (Sickness Impact Profile scale), survival and adverse events. Data collection and analysis: We identified three randomised clinical trials.Only two were included in the analysis. Each author graded the studies for methodological quality. Data were extracted and entered by the lead author and checked by the other two. Some missing data had to be regenerated by calculations based on ruler measurements of data presented in published graphs. Main results: In a European trial with 59 participants on placebo and 124 on rhIGF-I, 0.1 mg/kg/day the mean difference (MD) in change in AALSRS total score after nine months was -3.30 (95%confidence interval (CI) -8.68 to 2.08), non-significantly less in the treated than the placebo group. In a North American trial, in which 90 participants on placebo were compared with 89 on recombinant human insulin-like growth factor I 0.05 mg/kg/day, and 87 participants on 0.1 mg/kg/day, the MD after nine months was -6.00 (95%CI - 10.99 to -1.01), significantly less on treatment. The combined analysis from both randomised clinical trials showed a weighted mean difference after nine months of -4.75 (95% CI -8.41 to -1.09), a significant difference in favour of the treated group. The secondary outcome measures showed non-significant trends favouring rhIGF-I. Similarly the data with the 0.05 mg/kg/day dose showed trends favouring rhIGF-I at all time points but did not reach significance at the five per cent level at any point. There was an increased risk of injection site reactions with rhIGF-I (relative risk 2.53, 95% CI 1.40 to 4.59). Authors' conclusions: The available randomised placebo controlled trials do not permit a definitive assessment of the clinical efficacy of rhIGF-I on ALS. More research is needed and one trial is in progress. Future trials should include survival as an outcome measure. Copyright © 2008 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

23.	Fuster Torres MA, Berini Aytes L, Gay Escoda C. **Salivary gland application of botulinum toxin for the treatment of sialorrhea**. Medicina Oral, Patologia Oral y Cirugia Bucal 2007;12(7):E511-517.	Abstract: Sialorrhea or excessive salivation, and drooling, are common and disabling manifestations in different neurological disorders. A review is made of the literature, based on a PubMed search, selecting those articles describing clinical trials involving the injection of botulinum toxin A in the salivary glands of patients with different diseases characterized by sialorrhea. The most frequently treated diseases were infant cerebral palsy (30%), Parkinson's disease (20%) and amyotrophic lateral sclerosis (15%). Over half of the authors injected the product into the parotid glands, 9.5% into the submaxillary glands, and 38% into both. The total doses of toxin injected varied from 10-100 units of Botox or 30-450 units of Dysport according to the different authors. A reduction was observed in the production of saliva following these injections, and the duration of the therapeutic effect was 1.5-6 months. Six articles (30%) described the presence of adverse effects such as dysphagia, xerostomia and chewing difficulties. Most of the clinical studies involved small patient samples, with no blinding or randomization, and no control group. Moreover, no data are available on the efficacy and adverse effects of treatment in the context of long-term prospective studies. The effective therapeutic dose and ideal form of application remain to be established, and require the conduction of further controlled clinical trials involving large sample sizes.
24.	Benatar M. **Lost in translation: treatment trials in the SOD1 mouse and in human ALS**. Neurobiology of Disease 2007;26(1):1-13.	Abstract: Therapeutic success in the superoxide dismutase (SOD1) mouse model of amyotrophic lateral sclerosis (ALS) has not translated into effective therapy for human ALS, calling into question the utility of such preclinical data for identifying therapeutic agents that are worthy of further study in humans. This random effects meta-analysis of treatment trials in the superoxide dismutase (SOD1) mouse was undertaken in order to explore possible reasons for this failure of translational research and to identify potential pharmacological interventions that might be used in either a preventative or therapeutic trial in familial ALS. Among studies in which treatment was initiated presymptomatically, the weighted mean differences (WMDs) comparing the active treatment to control treated animals were 12 days (onset), 13 days (survival) and 5 days (survival interval). Among studies in which treatment was initiated at the time of symptom onset, the WMDs were 15 days (survival) and 8 days (survival interval). Subgroup analysis suggests that drugs such as minocycline and Cox-2 inhibitors with an anti-inflammatory mechanism of action, and anti-oxidative agents such as creatine or the manganese porphyrin AEOL-10150, appear to be the most promising for preventative and therapeutic trials respectively in patients with familial ALS. These conclusions should be tempered by the methodological limitations of the relevant literature.
25.	Hu J, Shi SG, Li LS. **Nervous system diseases and superoxide dismutase. [Chinese]**. Chinese Journal of Clinical	Abstract: Objective: To investigate the significance of superoxide dismutase (SOD) in the treatment and precaution of the occurrence of the nervous system diseases according to the recent studies at home and abroad about the role of free radicals in cerebral ischemia reperfusion, familial amyotrophic lateral scle-

	Rehabilitation 2005;9(33):130-132.	rosis, Parkinson disease, Alzheimer disease. Data sources: An online search of Medline database was undertaken by using the keywords of "superoxide dismutase, reperfusion after cerebral ischemia, familial amyotrophic lateral sclerosis, Parkinson disease, Alzheimer disease" to identify the relevant articles published in English from January 1997 to January 2005. Meanwhile, Chinese journals full-text database was scanned with computer to search relevant articles from January 1992 to January 2005, the keywords were "superoxide dismutase, reperfusion after cerebral ischemia, familial amyotrophic lateral sclerosis, Parkinson disease, Alzheimer disease" with language limited to Chinese. Study selection: Totally 120 articles were retrieved and screened, and 20 about SOD and nervous system diseases were selected, and then those with obvious indifferent contents or less correlation were excluded, and the full texts of the rest articles were searched to further identify the correlation. Inclusive criteria: randomized control trial; experimental or clinical study with parallel control group. Exclusive criteria: repetitive studies or reviews. Study extraction: The 20 articles were classified according to SOD and nervous system diseases, including 6 articles were correlated with reperfusion after cerebral ischemia, 8 with familial amyotrophic lateral sclerosis, 5 articles with Parkinson disease, and 7 with Alzheimer disease. Data synthesis: In the 20 articles, 650 patients or experiment animals were involved, it is significant that many kinds of nervous system diseases were caused by the increase of free radicals of in vivo superoxide anion, which leads to lipid peroxidation of biomembrane and lesion of DNA, and then results in the occurrences of various degenerated peuropathy. SOD can eliminate the damage caused by superoxide anion. Conclusion: As an important antioxidase, SOD has significance in the development of various nervous system diseases.
26.	Chou R, Peterson K, Helfand M. **Comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions: a systematic review**. Journal of Pain & Symptom Management 2004;28(2):140-175.	Abstract: Skeletal muscle relaxants are a heterogeneous group of medications used to treat two different types of underlying conditions: spasticity from upper motor neuron syndromes and muscular pain or spasms from peripheral musculoskeletal conditions. Although widely used for these indications, there appear to be gaps in our understanding of the comparative efficacy and safety of different skeletal muscle relaxants. This systematic review summarizes and assesses the evidence for the comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions. Randomized trials (for comparative efficacy and adverse events) and observational studies (for adverse events only) that included oral medications classified as skeletal muscle relaxants by the FDA were sought using electronic databases, reference lists, and pharmaceutical company submissions. Searches were performed through January 2003. The validity of each included study was assessed using a data abstraction form and predefined criteria. An overall grade was allocated for the body of evidence for each key question. A total of 101 randomized trials were included in this review. No randomized trial was rated good quality, and there was little evidence of rigorous adverse event assessment in included trials or observational studies. There is fair evidence that baclofen, tizanidine, and dantrolene are effective compared to placebo in

		patients with spasticity (primarily multiple sclerosis). There is fair evidence that baclofen and tizanidine are roughly equivalent for efficacy in patients with spasticity, but insufficient evidence to determine the efficacy of dantrolene compared to baclofen or tizanidine. There is fair evidence that although the overall rate of adverse effects between tizanidine and baclofen is similar, tizanidine is associated with more dry mouth and baclofen with more weakness. There is fair evidence that cyclobenzaprine, carisoprodol, orphenadrine, and tizanidine are effective compared to placebo in patients with musculoskeletal conditions (primarily acute back or neck pain). Cyclobenzaprine has been evaluated in the most clinical trials and has consistently been found to be effective. There is very limited or inconsistent data regarding the effectiveness of metaxalone, methocarbamol, chlorzoxazone, baclofen, or dantrolene compared to placebo in patients with musculoskeletal conditions. There is insufficient evidence to determine the relative efficacy or safety of cyclobenzaprine, carisoprodol, orphenadrine, tizanidine, metaxalone, methocarbamol, and chlorzoxazone. Dantrolene, and to a lesser degree chlorzoxazone, have been associated with rare serious hepatotoxicity.
27.	Parton M, Mitsumoto H, Leigh PN. **Amino acids for amyotrophic lateral sclerosis / motor neuron disease**. Cochrane Database of Systematic Reviews 2003(4):CD003457.	BACKGROUND: Amyotrophic lateral sclerosis, also known as motor neuron disease, is a progressive neuromuscular disease that causes disability and eventual death. Various amino acid preparations, the three branched-chain amino acids (L-leucine, L-valine and L-isoleucine) or, alternatively, L-threonine have been used as experimental therapy. OBJECTIVES: To examine the efficacy of amino acid therapies in prolonging survival and/or slowing the progression of amyotrophic lateral sclerosis/motor neuron disease. SEARCH STRATEGY: We searched the Cochrane Neuromuscular Disease Group trials register (searched February 2003), MEDLINE (from January 1966 to December 2002) and EMBASE (from January 1980 to December 2002) databases and reports of specialist conferences. Authors of known studies were contacted. SELECTION CRITERIA: We included randomised or quasi-randomised trials of participants with a clinical diagnosis of amyotrophic lateral sclerosis/motor neuron disease treated with all combinations of amino acids. Our primary outcome measure was survival determined by a pooled hazard ratio of all studies. Our secondary outcome measures were (in order of priority): survival at six and 12 months, muscle strength, any validated rating scale of physical function, quality of life, proportion of patients completing therapy and proportion of patients reporting adverse events attributable to treatment. DATA COLLECTION AND ANALYSIS: We identified six eligible trials and rejected a further seven because of incomplete data or inadequate duration. Eligible studies were rated for methodological quality and missing data sought from the authors. After this examination two studies were excluded from analysis.

		Our pooled survival analysis was performed by the Parmar method, other statistical calculations were done using the Review Manager 4.2 software package. MAIN RESULTS: No benefit could be demonstrated for either branched-chain amino acids or L-threonine in improving survival in amyotrophic lateral sclerosis/motor neuron disease. Neither could we find evidence of an effect of either treatment on muscle strength or disability as measured by functional rating scales. No study assessed quality of life. Both branched-chain amino acids and L-threonine appeared well tolerated and caused a degree of adverse events comparable to that of the control medication. REVIEWER'S CONCLUSIONS: There is no evidence to support a beneficial effect of either branched-chain amino acids or L-threonine in amyotrophic lateral sclerosis/motor neuron disease.
28.	Miller RG, Mitchell JD, Lyon M, Moore DH. **Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND)**. Amyotrophic Lateral Sclerosis & Other Motor Neuron Disorders 2003;4(3):191-206.	BACKGROUND: Riluzole 100 mg probably prolongs survival in patients with amyotrophic lateral sclerosis by about two months and the safety of the drug is not a major concern. The evidence from randomized controlled trials indicates that patients taking riluzole probably survive longer than patients taking placebo. The beneficial effects are very modest and the drug is expensive. Adverse effects from riluzole are relatively minor and for the most part reversible after stopping the drug. Riluzole has been approved for treatment of patients with amyotrophic lateral sclerosis in many countries but not all. Questions persist about its clinical utility because of high cost, modest efficacy and concern over adverse effects. OBJECTIVES: To examine the efficacy of riluzole in prolonging survival, and in delaying the use of surrogates (tracheostomy and mechanical ventilation) to sustain survival. SEARCH STRATEGY: Search of the Cochrane Neuromuscular Disease Group Register for randomized trials and enquiry from authors of trials, Aventis (manufacturer of riluzole) and other experts in the field. The most recent search was November 2002. SELECTION CRITERIA: Randomized trials of adults with diagnosis of amyotrophic lateral sclerosis (ALS), treated with riluzole or placebo. Types of outcome measures: Primary: pooled hazard ratio of tracheostomy-free survival over all time points with riluzole 100 mg. Secondary: per cent mortality as a function of time with riluzole 100 mg and other doses of riluzole; neurologic function, quality of life, muscle strength and adverse events. DATA COLLECTION & ANALYSIS: We identified four eligible randomized trials. Each reviewer graded them for methodological quality. Data extraction was performed by a single reviewer and checked by two others. We obtained some missing data from investigators and regulatory agencies. We performed meta-analyses with Review Manager 4.1 software using a fixed effects model. A test of drug efficacy was based on the Parmar pooled hazard ratio. RESULTS: The three trials examining tracheostomy-free survival included a total of 876 riluzole treated patients and 406 placebo treated patients. The data for tracheostomy-free survival was not available

		from the fourth trial. The methodological quality was acceptable and the three trials were easily comparable, although one trial included older patients in more advanced stages of amyotrophic lateral sclerosis. Riluzole 100 mg per day provided a benefit for the homogeneous group of patients in the first two trials (p=0.039, hazard ratio 0.80, 95% confidence interval 0.64 to 0.99) and there was no evidence of heterogeneity (p=0.33). When the third trial (which included older and more seriously affected patients) is added, there is evidence of heterogeneity (p<0.0001) and the random effects model, which takes this into account results in the overall treatment effect estimate falling just short of significance (p=0.056, hazard ratio 0.84, 95% confidence interval 0.70 to 1.01). This represents a 9% gain in the probability of surviving one year (57% in the placebo and 66% in the riluzole group). In secondary analyses of survival at separate time points, there was a significant survival advantage with riluzole 100 mg at six, nine, 12 and 15 months, but not at three or 18 months. There was a small beneficial effect on both bulbar and limb function, but not on muscle strength. There were no data on quality of life, but patients treated with riluzole remained in a more moderately affected health state significantly longer than placebo-treated patients (weighted mean difference 35.5 days, 95% confidence interval 5.9 to 65.0). A threefold increase in serum alanine transferase was more frequent in riluzole treated patients than controls (weighted mean difference 2.69, 95% confidence interval 1.65 to 4.38). CONCLUSIONS: Riluzole 100 mg daily is reasonably safe and probably prolongs survival by about two months in patients with ALS. More studies are needed, especially to clarify its effect in older patients (over 75 years), and those with more advanced disease.
29.	Garces K, Husereau D, Skidmore B, Turnbull J. **Riluzole for the treatment of amyotryophic lateral sclerosis: an assessment of clinical efficacy and safety**. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA); 2003.	Riluzole has the potential to reduce serious morbidity in certain patients at the cost of causing some drug intolerance (withdrawals due to adverse events). There is no information available to describe its impact on quality of life or time to tracheostomy alone. Overall objective: to assess the potential benefits and harms of riluzole for the treatment of patients with ALS. Specific objectives: to assess the effect of riluzole on mortality, morbidity, and quality of life for patients with ALS.
30.	Stewart A, Sandercock J, Bryan S, Hyde C, Barton PM, Fry-Smith A, et al. **The clinical effectiveness and cost-**	Sammendrag ikke tilgjengelig.

	effectiveness of riluzole for motor neurone disease: a rapid and systematic review. Health Technology Assessment (Winchester, England) 2001;5(2):1-97.	

Menneske-maskin interaksjon

Tab. 8: Systematiske oversikter om effekten av ulike former for menneske-maskin interaksjon

	Referanse	Sammendrag
1.	Marchetti M, Priftis K. **Brain-computer interfaces in amyotrophic lateral sclerosis: A metanalysis**. Clinical Neurophysiology 2015;126(6):1255-1263.	Objective: Despite recent groundbreaking findings on the genetic causes of amyotrophic lateral sclerosis (ALS), and improvements on neuroimaging techniques for ALS diagnosis have been reported, the main clinical intervention in ALS remains palliative care. Brain-computer interfaces (BCIs) have been proposed as a channel of communication and control for ALS patients. The present metanalysis was performed to test the evidence of BCI effectiveness in ALS, and to investigate whether the promising aims emerged from the first studies have been reached. Methods: Studies on ALS patients tested with BCIs, until June 2013, were searched in PubMed and PsychInfo. The random-effect approach was used to compute the pooled effectiveness of BCI in ALS. A meta-regression was performed to test whether there was a BCI performance improvement as a function of time. Finally, BCI effectiveness for complete paralyzed ALS patients was tested. Twenty-seven studies were eligible for metanalysis. Results: The pooled classification accuracy (C.A.) of ALS patients with BCI was about 70%, but this estimation was affected by significant heterogeneity and inconsistency. C.A. did not significantly increase as a function of time. C.A. of completely paralyzed ALS patients with BCI did not differ from that obtained by chance. Conclusions: After 15. years of studies, it is as yet not possible to reliably establish the effectiveness of BCIs. Significance: Methodological issues among the retrieved studies should be addressed and new well-powered studies should be conducted to confirm BCI effectiveness for ALS patients.
2.	Marchetti M, Priftis K. **Effectiveness of the P3-speller**	A quarter of century ago, Farwell and Donchin (1988) described their mental prosthesis for "talking off the top of your head." This innovative communication system, later named P3-speller, has been the most investigated and tested brain-computer inter-

	in brain-computer interfaces for amyotrophic lateral sclerosis patients: A systematic review and meta-analysis. Frontiers in Neuroengineering 2014;7(MAY).	face (BCI) system, to date. A main goal of the research on P3-spellers was the development of an effective assistive device for patients with severe motor diseases. Among these patients are those affected by amyotrophic lateral sclerosis (ALS). ALS patients have become a target population in P3-speller (and more generally in BCI) research. The P3-speller relies on the visual sensory modality, and it can be controlled by requiring users to actively move their eyes. Unfortunately, eye-movement control is usually not spared in the last stages of ALS, and, then, it is definitively lost in the case of complete paralysis. We reviewed the literature on ALS patients tested by means of P3-speller systems. Our aim was to investigate the evidence available to date of the P3-spellers effectiveness in ALS patients. To address this goal, a meta-analytic approach was adopted. The pooled classification accuracy performance, among retrieved studies, was about 74%. This estimation, however, was affected by significant heterogeneity and inconsistency among studies. This fact makes this percentage estimation (i.e., 74%) unreliable. Nowadays, the conclusion is that the initial hopes posed on P3-speller for ALS patients have not been met yet. In addition, no trials in which the P3-speller has been compared to current assistive technologies for communication (e.g., eye-trackers) are available. In conclusion, further studies are required to obtain a reliable index of P3-speller effectiveness in ALS. Furthermore, comparisons of P3-speller systems with the available assistive technologies are needed to assess the P3-speller usefulness with non-completely paralyzed ALS-patients. © 2014 Marchetti and Priftis.

Musikkterapi

Tab. 9: Systematisk oversikt om effekten av musikkterapi

	Referanse	Sammendrag
1.	Raglio A, Attardo L, Gontero G, Rollino S, Groppo E, Granieri E. **Effects of music and music therapy on mood in neurological patients**. World Journal of Psychiatry 2015;5(1):68-78.	Mood disorder and depressive syndromes represent a common comorbid condition in neurological disorders with a prevalence rate that ranges between 20% and 50% of patients with stroke, epilepsy, multiple sclerosis, and Parkinson's disease. Notwithstanding, these conditions are often under-diagnosed and under-treated in the clinical practice and negatively affect the functional recovery, the adherence to treatment, the quality of life, and even the mortality risk. In addition, a bidirectional association between depression and neurological disorders may be possible being that depressive syndromes may be considered as a risk factor for certain neurological diseases. Despite the large amount of evidence regarding the effects of music therapy

		(MT) and other musical interventions on different aspects of neurological disorders, no updated article reviewing outcomes such as mood, emotions, depression, activity of daily living and so on is actually available; for this reason, little is known about the effectiveness of music and MT on these important outcomes in neurological patients. The aim of this article is to provide a narrative review of the current literature on musical interventions and their effects on mood and depression in patients with neurological disorders. Searching on PubMed and PsycInfo databases, 25 studies corresponding to the inclusion criteria have been selected; 11 of them assess the effects of music or MT in Dementia, 9 explore the efficacy on patients with Stroke, and 5 regard other neurological diseases like Multiple Sclerosis, Amyotrophic Lateral Sclerosis/motor neuron disease, Chronic quadriplegia, Parkinson's Disease, and Acquired Brain dysfunctions. Selected studies are based on relational and rehabilitative music therapy approaches or concern music listening interventions. Most of the studies support the efficacy of MT and other musical interventions on mood, depressive syndromes, and quality of life on neurological patients.

Organisering

Tab. 10: Systematisk oversikt om effekten av «advance care planning» (ACP)

	Referanse	**Sammendrag**
1.	Murray L, Butow PN. Advance care planning in motor neuron disease: A systematic review. Palliat Support Care 2015:1-22.	OBJECTIVE: Motor neuron disease (MND) is an incurable progressive illness, characterized by incessant deterioration of neuromuscular function. Timely commencement of advance care planning (ACP) may enable patients to participate in future care choices. The present systematic review aimed to summarize what is known about the prevalence, content, patient/caregiver benefits, healthcare professional (HCP) awareness/support, and healthcare outcomes associated with ACP in the MND setting. METHOD: Quantitative and qualitative studies were identified through database searches and eligibility assessed by one author and verified by her coauthor. Data extraction and quality assessments against standardized criteria were completed by the two authors. RESULTS: Of the 422 studies identified, 16 were included. The research methods generally lacked rigor. Advance directive (AD) prevalence varied considerably across studies. Disease progression was the strongest predictor of AD completion. ACP processes may clarify patients' wishes and promote communication. HCP attitudes or lack of awareness may limit ACP processes. Varying patient preferences may make flexible approaches and timing necessary. SIGNIFICANCE OF RESULTS: Important

		benefits may be associated with ACP in the context of a motor neuron disease (e.g., feelings of control/relief and refusal of unwanted treatments). However, further evidence is required to verify findings and identify optimal streamlined approaches (e.g., use of decision aids) consistent with patients' (and caregivers') needs over time.

Psykologiske tiltak

Tab. 11: Systematisk oversikt om effekten av psykologisk behandling

	Referanse	Sammendrag
1.	Galante E, Gazzi L, Caffarra S. **Psychological activities in neurorehabilitation: from research to clinical practice**. Giornale Italiano di Medicina del Lavoro Ed Ergonomia 2011;33(1 Suppl A):A19-28.	The goal of the present review was to present a critical description of psychological research and practice in neurorehabilitation with regard to the efficacy of treatments proposed in the clinical and neuropsychological field. PubMed, Web of Science and Cochrane databases were searched by using the keywords "psychological intervention" and one of the following neurological diseases: "stroke", "TBI", "Parkinson", "ALS", "multiple sclerosis", "dementia". Randomized and pseudo-randomized trials, reviews and single case studies were included. We identified 134 papers: 54 concerning dementia, 24 stroke, 20 multiple sclerosis, 16 Parkinson, 13 TBI and 7 ALS. Most of these papers concern the evaluation of the effectiveness of psychological treatments in chronic or progressive neurological diseases. However, they are often characterized by methodological limitations, such as a small sample size, absence of a follow-up study or a control group. Further, high quality studies could help better understand treatment effects. There was some evidence for effectiveness of cognitive-behavioural and cognitive therapies, often applied both in clinical and neuropsychological interventions. Evidence coming from individualized treatment and single case studies are also described. In line with the data collected, we summarize some evidence available for psychological testing and treatment and argue that a multidisciplinary approach and a multidimensional evaluation should be adopted. According to this position, both randomized trials and single-case studies could be taken into account. Finally, it is proposed that in order to establish the efficacy of a given treatment, both standardized and individualized measures are to be used.

Spyttsekresjon

Tab. 12: Systematiske oversikter om effekten av ulike tiltak mot spyttsekresjon

	Referanse	Sammendrag
1.	Hawkey NM, Zaorsky NG, Galloway TJ. **The role of radiation therapy in the management of sialorrhea: A systematic review**. Laryngoscope 2015. Jul 7. doi: 10.1002/lary.25444. [Epub ahead of print]	PURPOSE: Up to 80% of patients with Parkinson disease and 30% of patients with amyotrophic lateral sclerosis (ALS) suffer from sialorrhea. Patients who fail medical and surgical therapy should be considered for external beam radiation therapy (EBRT). In this study, we conduct a systematic review to determine the dose and techniques used that result in greatest efficacy and lowest toxicity for the administration of EBRT in patients with Parkinson disease or ALS-associated sialorrhea. METHODS AND MATERIALS: This review included 216 patients from four prospective and six retrospective studies published from 1998 to 2014, with ALS or Parkinson disease who were treated with electron or photon EBRT for sialorrhea. RESULTS: A total of 216 patients were treated with EBRT from 10 studies. The indication for EBRT was failure of alternative medical treatment in all ALS patients. For patients with Parkinson disease, EBRT was the primary mode of treatment in 68% of cases. Overall, 176 (81%) of 216 patients treated with EBRT for sialorrhea reported symptomatic improvement from baseline. The most common target was the inferior two-thirds of the bilateral parotid glands and the entire bilateral submandibular glands. The total number of patients who experienced short-term toxicity was 86 of 216 patients (40%). The total number of patients who experienced long-term toxicity was 24 of 207 (12%). CONCLUSIONS: EBRT is an effective treatment for sialorrhea in patients suffering from ALS or Parkinson disease. Treatment to the bilateral submandibular glands and caudal parotid glands is the most common field arrangement. LEVEL OF EVIDENCE: NA Laryngoscope, 2015.
2.	Slade A, Stanic S. **Managing excessive saliva with salivary gland irradiation in patients with amyotrophic lateral sclerosis**. Journal of the Neurological Sciences 2015;352(1-2):34-36.	OBJECTIVE: A significant fraction of patients with amyotrophic lateral sclerosis (ALS) are unable to swallow saliva, which may result in the spillage of saliva outside of the oral cavity. Although anticholinergic agents and botulin toxin injections are considered the first line of treatment, they have not been effective for all patients. We performed a literature search on therapeutic salivary gland irradiation in patients with ALS. METHODS: We searched the PubMed for English language publications up to December 2014 on therapeutic salivary gland irradiation in patients with ALS. The search was performed using the following key words: amyotrophic lateral sclerosis, excessive salivation, sialorrhea, and radiation therapy.

		RESULTS: The majority of ALS patients with excessive salivation respond well to salivary gland irradiation. The whole bilateral submandibular, and whole or partial bilateral parotid glands have been the target tissue for radiation therapy in most of the published studies. Various radiation therapy regimens have been utilized. The response to radiation therapy lasts for several months. CONCLUSIONS: The majority of ALS patients with excessive salivation respond well to salivary gland irradiation. Neurologists should consider this treatment option for select patients with ALS and excessive salivation.
3.	Young CA, Ellis C, Johnson J, Sathasivam S, Pih N. **Treatment for sialorrhea (excessive saliva) in people with motor neuron disease/amyotrophic lateral sclerosis**. Cochrane Database of Systematic Reviews 2011(5):CD006981.	BACKGROUND: Motor neuron disease (MND), also known as amyotrophic lateral sclerosis, is a progressive, neurodegenerative condition which may cause dysphagia, as well as limb weakness, dysarthria, emotional lability and respiratory failure. Since normal salivary production is 0.5 to 1.5 litres daily, loss of salivary clearance due to dysphagia leads to salivary pooling and sialorrhea, often resulting in distress and inconvenience to patients. OBJECTIVES: To systematically review evidence on treatment of sialorrhea in MND, including medications, radiotherapy and surgery. SEARCH STRATEGY: We searched the Cochrane Neuromuscular Disease Group Specialized Register (1 October 2010), the Cochrane Central Register of Controlled Trials)(CENTRAL) (The Cochrane Library issue 3, 2010), MEDLINE (January 1966 to September 2010), EMBASE (January 1980 to September 2010), AMED (1985 to September 2010) and CINAHL Plus (January 1937 September 2010). All bibliographies of the identified randomized trials were reviewed and authors contacted as needed. Known experts in the field were contacted to identify further published and unpublished papers. SELECTION CRITERIA: We included randomized and quasi-randomised controlled studies on any intervention for sialorrhea and related symptoms, in people with MND. DATA COLLECTION AND ANALYSIS: Review authors summarised data independently in a customised data collection form and confirmed data presented in Cochrane Review Manager software. MAIN RESULTS: Only one randomized controlled trial was identified. This was a well designed study of botulinum toxin B injected into parotid and submandibular glands of 20 patients, which showed positive results for four weeks (Jackson 2009). There was low risk of bias in the study and no significant adverse events reported. AUTHORS' CONCLUSIONS: There is some evidence for use of botulinum toxin injections to salivary glands for the treatment of sialorrhea in MND. Further research is required on this important symptom. Data are needed on the problem of sialorrhea in MND and its measurement, both by patient self report measures and objective tests. These will allow the development of better randomized controlled trials.

4.	Stone CA, O'Leary N. **Systematic review of the effectiveness of botulinum toxin or radiotherapy for sialorrhea in patients with amyotrophic lateral sclerosis**. Journal of Pain & Symptom Management 2009;37(2):246-258.	Fifty percent of patients with amyotrophic lateral sclerosis (ALS) experience problems handling serous saliva and 20% fail to achieve adequate control of sialorrhea with anticholinergic medications, or experience intolerable adverse effects from these drugs. Both botulinum and radiotherapy have been suggested in the literature as treatments for intractable sialorrhea. In this review, we assess the evidence for the effectiveness and toxicity of botulinum toxin and radiotherapy for sialorrhea in patients with ALS. Relevant studies were retrieved from Medline, Embase and Cochrane Databases. Handsearching of Neurology, Journal of Pain and Symptom Management, and Palliative Medicine and of reference lists, was carried out. Five studies (28 patients) were included in the analysis of botulinum. Of the four studies using an intraglandular method of injection, no adverse effects occurred. Two of these had positive findings of the effect of botulinum in salivary secretion rate and quality of life. In contrast, significant adverse effects were experienced by two patients in a study of retrograde injections into the salivary ducts. Two studies were included in the analysis of radiotherapy (27 patients). Both demonstrated a positive effect of radiotherapy on salivary secretion rate. Some patients experienced mild acute side effects. Because of the small numbers of studies, small sample sizes, and poor quality of reporting, it is not possible to draw firm conclusions. There is some evidence indicating that both botulinum and radiotherapy are well tolerated, effective treatments for persistent sialorrhea in patients with ALS and that the duration of action is up to three months with botulinum and six months with radiotherapy.
5.	Squires N, Arthur A, Wills A. **Non-surgical treatments for drooling in MND/ALS: A systematic review**. Amyotrophic Lateral Sclerosis 2009;10:194-195.	Background: Bulbar weakness is the main presenting feature in approximately 25% of patients with MND/ALS. Drooling of saliva is a distressing symptom associated with bulbar dysfunction. This can have important physical, psychological and social effects on the individual and their family. Patients can experience thick mucoid secretions pooling in the oropharynx and/or thin watery saliva which leads to drooling. It is important to identify the type of difficulty experienced to guide intervention. Treatment approaches vary, therefore to improve patient care, disease-specific evidence-based guidelines are needed. Objectives: To assess the evidence to support current nonsurgical treatments to reduce drooling in MND/ALS. Methods: A systematic review of the treatment of drooling was carried out. Inclusion criteria were: 1) evaluations of nonsurgical interventions to reduce thin saliva in MND/ALS; 2) studies of more than two subjects; and 3) published in English language. The search strategy was divided into four steps 1) electronic search of four clinically relevant databases; 2) hand searches of all 19 International ALS/MND symposium journals; 3) an email request for unpublished studies sent to the 16 MND care centres in the UK and Ireland; and 4) hand searching of reference lists. Results: Of the 64 published reports identified on the basis of title and abstract, only 15 met the inclusion criteria. The methodological quality of these studies varied, only one was a randomised controlled trial. Of the 15 studies, 4 reported the use of radiation, 8 studies the use of botulinum toxin injections, 1 reported a combination of radiation and botulinum, 1 a comparison of botulinum and amitriptyline and 1 the sublingual administration of atropine. Sample sizes were small (n = 4 to n = 20). Outcomes included

		the weight of cotton wool, number of tissues used and patient rating scales. The average length of follow up varied between 2 and 80 weeks. Although all studies reported the intervention tested to be effective only 5 studies showed statistically significant changes. Discussion and Conclusions: Although many authors in the studies reviewed claimed that botulinum toxin injections and radiation are effective in reducing saliva in patients with MND/ALS, it has not been possible hitherto to demonstrate this with a definitive randomised controlled trial. While lack of consensus on the best treatment available for salivation in MND suggests that a trial could be justified on the basis of equipoise, recruiting sufficient patient numbers to detect important differences might be problematic. We argue that to achieve this goal, a consensus needs to be built on how to standardise treatments, and identify the most patient-centred and robust outcome. This will then allow for such treatments to be tested in an ethical manner in multiple centres to allow meaningful statistical interpretation.
6.	Stone C, O'Leary N. **Systematic review of the effectiveness of botulinum toxin and radiotherapy for sialorrhea in patients with amyotrophic lateral sclerosis**. J Pain Symptom Manag 2009;37(2):246-58.	Fifty percent of patients with amyotrophic lateral sclerosis (ALS) experience problems handling serous saliva and 20% fail to achieve adequate control of sialorrhea with anticholinergic medications, or experience intolerable adverse effects from these drugs. Both botulinum and radiotherapy have been suggested in the literature as treatments for intractable sialorrhea. In this review, we assess the evidence for the effectiveness and toxicity of botulinum toxin and radiotherapy for sialorrhea in patients with ALS. Relevant studies were retrieved from Medline, Embase and Cochrane Databases. Handsearching of Neurology, Journal of Pain and Symptom Management, and Palliative Medicine and of reference lists, was carried out. Five studies (28 patients) were included in the analysis of botulinum. Of the four studies using an intraglandular method of injection, no adverse effects occurred. Two of these had positive findings of the effect of botulinum in salivary secretion rate and quality of life. In contrast, significant adverse effects were experienced by two patients in a study of retrograde injections into the salivary ducts. Two studies were included in the analysis of radiotherapy (27 patients). Both demonstrated a positive effect of radiotherapy on salivary secretion rate. Some patients experienced mild acute side effects. Because of the small numbers of studies, small sample sizes, and poor quality of reporting, it is not possible to draw firm conclusions. There is some evidence indicating that both botulinum and radiotherapy are well tolerated, effective treatments for persistent sialorrhea in patients with ALS and that the duration of action is up to three months with botulinum and six months with radiotherapy.

Stamcellebehandling

Tab. 13: Systematiske oversikter om effekten av stamcellebehandling

	Referanse	Sammendrag
1.	Jeong H, Yim HW, Cho YS, Kim HB, Oh IH, Jeong S. **Systematic review and meta-analysis of efficacy and safety of stem cell therapy in amyotrophic lateral sclerosis**. Cyto-therapy 2015;1):S55-S56.	Stem cell therapy may be promising options for the treatment of ALS. However, the effects of these treatments are not yet fully understood and there is a lack of firm evidence on the efficacy of stem cell therapy for those patients due to the absence of sufficiently powered randomized controlled trials. Therefore, we performed a meta-analysis of available single-arm studies using stem cell based therapy in patients with ALS. A systematic search and critical review of the literature published from its inception through February 2013 was performed. The articles included in the search were restricted to the English language, studies with at least 5patients, 3 or more month follow-up, and efficacy evaluation using ALSFRS. Article selection and data extraction were conducted by two authors independently with standard methods. Data analyses were performed using Comprehensive Meta-analysis version 2.2. (Biostat Inc., Englewood, NJ). We conducted fixed or random effects model meta-analyses to assess efficacy outcomes. The quality of studies was assessed using the Newcastle-Ottawa Scale. We included 11 studies in the single arm meta-analysis. The pooled mean difference in ALS-FRS from the baseline to primary end points was decreased by 3.3points (95% CI: -5.38 to -1.22) in which ALS-FRS declined 0.4 points permonth. In terms of FVC, the pooled mean difference from the baseline was decreased by 14%(95% CI: -19 to -6%), average decline in FVC was 1.2% per month. According to natural history data, ALS-FRS score was declined 1.01 points and FVC reduced 2.7% and per month in patients with ALS. Compared to natural history stem cell therapy for patients with ALS can be judged as slowing the disease progression based on single arm clinical studies. However, clinical benefits of stem cell therapy for patients with ALS need further investigation and reevaluation to test the clinical efficacy.
2.	Alvarim LT, Nucci LP, Mamani JB, Marti LC, Aguiar MF, Silva HR, et al. **Therapeutics with SPION-labeled stem cells for the main diseases related to brain aging: a**	The increase in clinical trials assessing the efficacy of cell therapy for structural and functional regeneration of the nervous system in diseases related to the aging brain is well known. However, the results are inconclusive as to the best cell type to be used or the best methodology for the homing of these stem cells. This systematic review analyzed published data on SPION (superparamagnetic iron oxide nanoparticle)-labeled stem cells as a therapy for brain diseases, such as ischemic stroke, Parkinson's disease, amyotrophic lateral sclerosis, and dementia. This review highlights the therapeutic role of stem cells in reversing the aging process and the pathophysiology of brain aging, as well as emphasizing nanotechnology as an important tool to monitor stem cell migration in affected regions of the brain.

	systematic review. International Journal of Nanomedicine 2014;9:3749-3770.	
3.	Pallotta R, Andrade A, Paiva CM. **Cell therapy in amyotrophic lateral sclerosis. [Portuguese]**. Revista Neurociencias 2010;18(2):256-266.	Introduction. The amyotrophic lateral sclerosis is the most common motor neuron disease in adults, with poor prognosis and limited treatment options, which leads to exploration of alternative therapies. Method. This paper, through a literature review, seeks to describe the advances in the use of stem cells in treatment of amyotrophic lateral sclerosis. Results. Twelve articles in animal models and 8 clinical trials in human models were analyzed, and observed either clinical improvement or stagnation of the disease in most of the cases. No worsening was related to the procedure, but some questions have not been elucidated, such as the best source of cells to be used, the most appropriate way to infuse, the population to be benefited, and the need or not to use immunosuppression therapy prior to the infusion. Conclusion. Thus we can conclude that cell therapy has a great therapeutic potential, but new clinical trials should be developed in order to clarify these remaining questions.

Søvnproblemer

Tab. 14: Systematiske oversikter om effekten av tiltak mot søvnproblemer

	Referanse	Sammendrag
1.	Lin X, Li J, Liu L. **Evidence-based therapy for sleep disorders in neurodegenerative diseases. [Chinese]**. Chinese Journal of Contemporary Neurology and Neurosurgery 2013;13(8):691-696.	Objective: To evaluate the effectiveness of the treatments for sleep disorders in neurodegenerative diseases so as to provide the best therapeutic regimens for the evidence-based treatment. Methods: Search PubMed, MEDLINE, Cochrane Library, Wanfang Data and China National Knowledge Infrastructure (CNKI) databases with "sleep disorder or sleep disturbance", "neurodegenerative diseases", "Parkinson's disease or PD", "Alzheimer's disease or AD", "multiple system atrophy or MSA" as retrieval words. The quality of the articles were evaluated with Jadad Scale. Results: A total of 35 articles, including 2 systematic reviews, 5 randomized controlled trials, 13 clinical controlled trials, 13 case series and 2 epidemiological investigation studies were included for evaluation, 13 of which were high grade and 22 were low grade articles. Clinical evidences showed that: 1) advice on sleep hygiene, careful use of

		dopaminergic drugs and hypnotic sedative agents should be considered for PD. Bright light therapy (BLT) may improve circadian rhythm sleep disorders and clonazepam may be effective for rapid eye movement sleep behavior disorder (RBD). However, to date, very few controlled studies are available to make a recommendation for the management of sleep disorders in PD; 2) treatments for sleep disorders in AD include drug therapy (e.g. melatonin, acetylcholinesterase inhibitors, antipsychotic drugs, antidepressants) and non-drug therapy (e.g. BLT, behavior therapy), but very limited evidence shows the effectiveness of these treatments; 3) the first line treatment for sleep-related breathing disorder in MSA is nasal continuous positive airway pressure (nCPAP), and clonazepam is effective for RBD in MSA; 4) there is rare evidence related to the treatment of sleep disorders in dementia with Lewy body (DLB) and amyotrophic lateral sclerosis (ALS). Conclusion: Evidence-based medicine can provide the best clinical evidence on sleep disorders' treatment in neurodegenerative diseases.

Tale

Tab. 15: Systematisk oversikt om effekten av tiltak mot taleproblemer

	Referanse	Sammendrag
1.	Hanson EK, Yorkston KM, Britton D. **Dysarthria in amyotrophic lateral sclerosis: A systematic review of characteristics, speech treatment and augmentative and alternative communication options**. Journal of Medical Speech-Language Pathology 2011;19(3):12-30.	This evidence-based review addresses intervention and management of dysarthria related to amyotrophic lateral sclerosis (ALS; Lou Gehrig's disease) and is part of a series of evidence-based systematic reviews sponsored by the Academy of Neurologic Communication Disorders and Sciences. A search of electronic databases (PsychINFO, Medline, and CINAHL) and hand search of relevant edited books yielded 713 articles on the topics related to characteristics, intervention, and management of the dysarthrias associated with ALS. This review summarizes the characteristics of dysarthria in ALS and appraises and summarizes findings from studies investigating speech treatment and augmentative and alternative communication (AAC) interventions for people with ALS. Findings include (1) well-documented characteristics of the progressive, mixed spastic and flaccid dysarthria; (2) consensus of expert opinion indicating the benefits of communication strategies, including speech supplementation and partner training for mild to moderate dysarthria; (3) a lack of evidence supporting the use of strengthening exercises for improving speech; (4) usefulness of monitoring of rates of speech to predict intelligibility declines and thus inform the timing of AAC intervention; (5) emerging evidence of the long-term usefulness of AAC systems; and (6) the influence of other factors, such as cognitive decline, that may affect the success of various interventions. Copyright © 2011 Delmar Cengage Learning.

Transkraniell magnetisk stimulering

Tab. 16: Systematisk oversikt om effekten av transkraniell magnetisk stimulering

	Referanse	Sammendrag
1.	Fang J, Zhou M, Yang M, Zhu C, He L. **Repetitive transcranial magnetic stimulation for the treatment of amyotrophic lateral sclerosis or motor neuron disease**. Cochrane Database of Systematic Reviews 2013(5):CD008554.	BACKGROUND: Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease (MND), is a progressive neurodegenerative disease without effective therapies. Several studies have suggested that repetitive transcranial magnetic stimulation (rTMS) may have positive benefit in ALS. However, the efficacy and safety of this therapy remain uncertain. This is the first update of a review published in 2011. OBJECTIVES: To determine the clinical efficacy and safety of rTMS for treating ALS. SEARCH METHODS: On 30 July 2012, we searched the Cochrane Neuromuscular Disease Group Specialized Register, CENTRAL (2012, issue 7 in The Cochrane Library), MEDLINE (1966 to July 2012), EMBASE (1980 to July 2012), CINAHL (1937 to July 2012), Science Citation Index Expanded (January 1945 to July 2012), AMED (January 1985 to July 2012). We searched the Chinese Biomedical Database (1979 to August 2012). We also searched for ongoing studies on clinicaltrials.gov (August 2012). SELECTION CRITERIA: Randomised and quasi-randomised controlled trials assessing the therapeutic efficacy and safety of rTMS for patients with a clinical diagnosis of ALS.Comparisons eligible for inclusion were:1. rTMS versus no intervention;2. rTMS versus sham rTMS;3. rTMS versus physiotherapy;4. rTMS versus medications;5. rTMS + other therapies or drugs versus sham rTMS + the same therapies or drugs;6. different methods of application of rTMS such as high-frequency (> 1Hz) compared to low-frequency (< 1Hz) rTMS. DATA COLLECTION AND ANALYSIS: Two authors independently selected papers, assessed risk of bias and extracted data. We resolved disagreements through discussion. We contacted study authors for additional information. MAIN RESULTS: Three randomised, placebo-controlled trials with a total of 50 participants were included in the review. All three trials compared rTMS with sham TMS. All the trials were of poor methodological quality and were insufficiently homogeneous to allow the pooling of results. Moreover, the high rate of attrition further increased the risk of bias. None of the trials provided detailed data on the ALS Functional Rating Scale-Revised

		(ALSFRS-R) scores at six months follow-up which was pre-assigned as our primary outcome. One trial contained data in a suitable form for quantitative analysis of our secondary outcomes. No difference was seen between rTMS and sham rTMS using the ALSFRS-R scores and manual muscle testing (MMT) scores at 12 months follow-up in this trial. Additionally, none of the trials reported any adverse events associated with the use of rTMS. However, in view of the small sample size, the methodological limitations and incomplete outcome data, treatment with rTMS cannot be judged as completely safe. AUTHORS' CONCLUSIONS: There is currently insufficient evidence to draw conclusions about the efficacy and safety of rTMS in the treatment of ALS. Further studies may be helpful if their potential benefit is weighed against the impact of participation in a randomised controlled trial on people with ALS.

Tverrfaglig behandling

Tab. 17: Systematisk oversikt om effekten av tverrfaglig behandling («multidisciplinary care»)

	Referanse	Sammendrag
1.	Ng L, Khan F, Mathers S. **Multidisciplinary care for adults with amyotrophic lateral sclerosis or motor neuron disease**. Cochrane Database of Systematic Reviews 2009(4):CD007425.	Background: Multidisciplinary care (MDC) is increasingly thought to be an important means of symptomatic and supportive management formotor neuron disease (MND) but the evidence base for its effectiveness is unclear. Objectives: To assess the effectiveness of MDC in adults with MND, especially the types of approaches that are effective (settings, intensity) and the outcomes that are affected. Search strategy: We searched The Cochrane Neuromuscular Disease Group Specialized Register (11 May 2009), and The Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 2, 2009), MEDLINE (1966 to April 2009), EMBASE (1980 to April 2009), CINAHLPlus (1937 to April 2009), AMED (1985 to April 2009) and LILACS (1982 to April 2009). Selection criteria: Randomised and controlled clinical trials that compared MDC in MND with either routinely available local services or lower levels of intervention; or studies that compared MDC in different settings or at different levels of intensity. Studies of 'other designs' (such as observational studies) were included only in the Discussion since such studies could only be of limited contribution to the best evidence synthesis. Data collection and analysis: We performed a 'best evidence' synthesis based on methodological quality. We grouped studies in terms of setting and intensity (high or low) of therapy. Main results: No randomised controlled trials or controlled clinical trials were identified. We summarised the results of five observational studies (including one with two reports) in the

		Discussion section of this review. Authors' conclusions: In the absence of randomised controlled trials or controlled clinical trials, the 'best' evidence to date is based on three 'low' and two 'very low quality' observational studies. These suggest 'very low quality evidence' for an advantage for mental health domains (only) of quality of life without increasing healthcare costs, and 'low level quality' evidence for reduced hospitalisation for MDC in low-intensity outpatient settings; and 'very low quality' evidence for improved disability in high-intensity settings. The evidence for survival is conflicting. These conclusions are tentative and the gap in current research should not be interpreted as proof that MDC is ineffective. Further research is needed into appropriate study designs; outcome measurement; caregiver needs; and the evaluation of optimal settings, type, intensity or frequency and cost-effectiveness of MDC in the MND population. Future research should focus on observational designs to assess care and outcomes in 'real-life' settings. The interface between neurology, rehabilitation and palliative care should be explored to provide long-term support for MND. Copyright © 2009 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Ventilasjonsstøtte

Tab. 18: Systematiske oversikter om effekten av ulike former for ventilasjonsstøtte

	Referanse	Sammendrag
1.	**The effect of mechanical ventilation on quality of life in patients with motor neurone disease**. British Journal of Neuroscience Nursing 2015;11(5):220-227	Motor neurone disease (MND) is a neurodegenerative condition, which is characterised by a progressive muscle weakening. As the disease progresses, many patients will experience respiratory insufficiency, which is the main cause of death in MND. Non-invasive ventilation (NIV) and/or invasive ventilation (IV) via a tracheostomy can be used to palliate these distressing respiratory symptoms and maintain quality of life (QOL). The aim of this literature review is to establish whether the use of artificial ventilation improves and/or maintains QOL. Additional objectives of this review are to evaluate contemporary primary research investigating the impact of mechanical ventilation on QOL in MND and to identify any disadvantages of mechanical ventilation and

		how these could be overcome in future practice. The use of NIV/IV in MND has both positive and negative effects on overall QOL. More comprehensive research needs to be conducted to establish how optimal QOL can be maintained despites the progressive nature of MND.
2.	Mitre B, Davidson M, Daxberg E-L, Jivegård L, Rosén H, Svanberg T, et al. **Invasive ventilation in patients with amyotrophic lateral sclerosis and respiratory failure. Health Technology Assessment**. Västra Götalandsregionen, Sahlgrenska Universitetssjukhuset, HTA-centrum; 2014. (HTA-rapport 2014:72).	Sammendrag ikke tilgjengelig.
3.	Hannan LM, Dominelli GS, Chen YW, Darlene Reid W, Road J. Systematic review of non-invasive positive pressure ventilation for chronic respiratory failure. Respiratory Medicine 2014;108(2):229-243.	BACKGROUND: This systematic review examined the effect of non-invasive positive pressure ventilation (NIPPV) on patient reported outcomes (PROs) and survival for individuals with or at risk of chronic respiratory failure (CRF). METHODS: Randomised controlled trials (RCTs) and prospective non-randomised studies in those treated with NIPPV for CRF were identified from electronic databases, reference lists and grey literature. Diagnostic groups included in the review were amyotrophic lateral sclerosis/motor neuron disease (ALS/MND), Duchenne muscular dystrophy (DMD), restrictive thoracic disease (RTD) and obesity hypoventilation syndrome (OHS). RESULTS: Eighteen studies were included and overall study quality was weak. Those with ALS/MND had improved somnolence and fatigue as well as prolonged survival with NIPPV. For OHS, improvements in somnolence and fatigue, dyspnoea and sleep quality were demonstrated, while for RTD, measures of dyspnoea, sleep quality, physical function and health, mental and emotional health and social function improved. There was insufficient evidence to form conclusions regarding the effect of NIPPV for those with DMD.

CONCLUSIONS: This review has demonstrated that NIPPV influences PROs differently depending on the underlying cause of CRF. These findings may provide assistance to patients and clinicians to determine the relative costs and benefits of NIPPV therapy and also highlight areas in need of further research.

4.	Annane D, Orlikowski D, Chevret S. **Nocturnal mechanical ventilation for chronic hypoventilation in patients with neuromuscular and chest wall disorders**. Cochrane Database of Systematic Reviews 2014(12):CD001941.	BACKGROUND: Chronic alveolar hypoventilation is a common complication of many neuromuscular and chest wall disorders. Long-term nocturnal mechanical ventilation is commonly used to treat it. This is a 2014 update of a review first published in 2000 and previously updated in 2007. OBJECTIVES: To examine the effects on mortality of nocturnal mechanical ventilation in people with neuromuscular or chest wall disorders. Subsidiary endpoints were to examine the effects of respiratory assistance on improvement of chronic hypoventilation, sleep quality, hospital admissions and quality of life. SEARCH METHODS: We searched the Cochrane Neuromuscular Disease Group Specialized Register, CENTRAL, MEDLINE and EMBASE on 10 June 2014. We contacted authors of identified trials and other experts in the field. SELECTION CRITERIA: We searched for quasi-randomised or randomised controlled trials of participants of all ages with neuromuscular or chest wall disorder-related stable chronic hypoventilation of all degrees of severity, receiving any type and any mode of long-term nocturnal mechanical ventilation. The primary outcome measure was one-year mortality and secondary outcomes were unplanned hospital admission, short-term and long-term reversal of hypoventilation-related clinical symptoms and daytime hypercapnia, improvement of lung function and sleep breathing disorders. DATA COLLECTION AND ANALYSIS: We used standard Cochrane methodology to select studies, extract data and assess the risk of bias in included studies. MAIN RESULTS: The 10 eligible trials included a total of 173 participants. Roughly half of the trials were at low risk of selection, attrition or reporting bias, and almost all were at high risk of performance and detection bias. Four trials reported mortality data in the long term. The pooled risk ratio (RR) of dying was 0.62 (95% confidence interval (CI) 0.42 to 0.91, P value = 0.01) in favour of nocturnal mechanical ventilation compared to spontaneous breathing. There was considerable and significant heterogeneity between the trials, possibly related to differences between the study populations. Information on unplanned hospitalisation was available from two studies. The corresponding pooled RR was 0.25 (95% CI 0.08 to 0.82, P value = 0.02) in favour of nocturnal mechanical ventilation. For most of the outcome measures there was no significant long-term difference between nocturnal mechanical ventilation and no ventilation. Most of the secondary outcomes were not assessed in the eligible trials. Three out of the 10 trials, accounting for 39 participants, two with a cross-over design and one with two parallel groups, compared volume- and pressure-cycled non-invasive mechanical ventilation in the short term. From the only trial (16 participants) on parallel groups, there was no difference in mortality (one death in each arm) between volume- and pressure-cycled mechanical ventilation. Data from the two cross-over trials suggested that compared with pressure-cycled ventilation, volume-cycled ventilation was associated with less sleep time spent with an arterial oxygen saturation below 90% (mean difference (MD) 6.83 minutes, 95% CI 4.68 to 8.98, P value = 0.00001) and a lower apnoea-hypopnoea (per sleep hour)

index (MD -0.65, 95% CI -0.84 to -0.46, P value = 0.00001). We found no study that compared invasive and non-invasive mechanical ventilation or intermittent positive pressure versus negative pressure ventilation. AUTHORS' CONCLUSIONS: Current evidence about the therapeutic benefit of mechanical ventilation is of very low quality, but is consistent, suggesting alleviation of the symptoms of chronic hypoventilation in the short term. In four small studies, survival was prolonged and unplanned hospitalisation was reduced, mainly in participants with motor neuron diseases. With the exception of motor neuron disease and Duchenne muscular dystrophy, for which the natural history supports the survival benefit of mechanical ventilation against no ventilation, further larger randomised trials should assess the long-term benefit of different types and modes of nocturnal mechanical ventilation on quality of life, morbidity and mortality, and its cost-benefit ratio in neuromuscular and chest wall diseases.

5.	Radunovic A, Annane D, Rafiq MK, Mustfa N. **Mechanical ventilation for amyotrophic lateral sclerosis/motor neuron disease**. Cochrane Database of Systematic Reviews 2013(3):CD004427.	BACKGROUND: Amyotrophic lateral sclerosis, also known as motor neuron disease, is a fatal neurodegenerative disease. Neuromuscular respiratory failure is the commonest cause of death, usually within two to five years of the disease onset. Supporting respiratory function with mechanical ventilation may improve survival and quality of life. This is the first update of a review first published in 2009. OBJECTIVES: The primary objective of the review is to examine the efficacy of mechanical ventilation (tracheostomy and non-invasive ventilation) in improving survival in ALS. The secondary objectives are to examine the effect of mechanical ventilation on functional measures of disease progression and quality of life in people with ALS; and assess adverse events related to the intervention. SEARCH METHODS: We searched The Cochrane Neuromuscular Disease Group Specialized Register (1 May 2012), CENTRAL (2012, Issue 4), MEDLINE (January 1966 to April 2012), EMBASE (January 1980 to April 2012), CINAHL Plus (January 1937 to April 2012), and AMED (January 1985 to April 2012). We also searched for ongoing studies on ClinicalTrials.gov. SELECTION CRITERIA: Randomised and quasi-randomised controlled trials involving non-invasive or tracheostomy assisted ventilation in participants with a clinical diagnosis of amyotrophic lateral sclerosis, independent of the reported outcomes. We planned to include comparisons with no intervention or the best standard care. DATA COLLECTION AND ANALYSIS: For the original review, four authors independently selected studies for assessment and two authors reviewed searches for this update. All authors extracted data independently from the full text of selected studies and assessed the risk of bias in studies that met the inclusion criteria. We attempted to obtain missing data where possible. We planned to collect adverse event data from included studies. MAIN RESULTS: For the original Cochrane review, the review authors identified and included two randomised controlled trials involving 54 participants with ALS receiving non-invasive ventilation. There were no new randomised or quasi-randomised controlled trials at this first update.Incomplete data were published for one study and we contacted the trial authors who were not able to provide the missing data. Therefore, the results of the review were based on a single study of 41 participants that compared non-invasive ventilation with standard care. It was a well conducted study with low risk of bias.The study showed that the overall median survival was significantly different between the group treated with non-invasive ventilation and the standard care group. The median survival in the non-invasive ventilation group was 48 days longer (219 days compared to 171 days for the standard care group (estimated 95% CI 12 to 91 days, P = 0.0062)). This survival benefit was accompanied by an enhanced quality of life. On subgroup analysis, the survival and quality of life benefit was much more in the subgroup with normal to moderately impaired bulbar function (20 participants); median survival was 205 days longer (216 days in NIV group versus 11 days in the standard care group, P =

		0.0059). Non-invasive ventilation did not prolong survival in participants with poor bulbar function (21 participants), although it showed significant improvement in the mean symptoms domain of the Sleep Apnoea Quality of Life Index but not in the Short Form-36 Health Survey Mental Component Summary score. Neither trial reported clinical data on intervention related adverse effects. AUTHORS' CONCLUSIONS: Evidence from a single randomised trial of non-invasive ventilation in 41 participants suggests that it significantly prolongs survival and improves or maintains quality of life in people with ALS. Survival and some measures of quality of life were significantly improved in the subgroup of people with better bulbar function, but not in those with severe bulbar impairment. Future studies should examine the health economics of NIV and factors influencing access to NIV. We need to understand the factors, personal and socioeconomic, that determine access to NIV.
6.	Jones U, Enright S, Busse M. **Management of respiratory problems in people with neurodegenerative conditions: a narrative review**. Physiotherapy 2012;98(1):1-12.	BACKGROUND: Respiratory failure and dysfunction are common problems in many neurodegenerative conditions. Although physiotherapists manage these problems, it is not known which treatments have been studied and their efficacy. OBJECTIVE: To review evidence on the management of respiratory problems in people with neurodegenerative conditions using the PRISMA approach. DATA SOURCES: Comprehensive searches were conducted using the following electronic databases from inception to May 2010: HUGEnet, SIGLE, British Library Direct, CINAHL, Medline, AMED and Web of Knowledge. Bibliographies of all studies and systematic reviews were searched by hand. STUDY SELECTION: Studies were selected based on: self-ventilating participants with neurodegenerative conditions; interventions aimed at improving respiratory function; and any valid and reliable measures of respiratory function as outcomes. STUDY APPRAISAL: Studies were appraised by one reviewer using the Critical Appraisal Skills Programme. Data were synthesised using a narrative approach. RESULTS: Thirty-five studies were included in the review. The strongest evidence was for the use of non-invasive ventilation for people with amyotrophic lateral sclerosis, although this was weak. The evidence for the use of respiratory muscle training and methods to increase peak cough flow showed a positive effect, but was also weak. CONCLUSION: There is weak evidence for the positive effects of physiotherapeutic interventions for respiratory problems in people with neurodegenerative conditions. Further work is necessary in specific neurodegenerative conditions to identify why respiratory problems occur, and larger scale studies should be undertaken to investigate management of these problems.

7.	Brurberg KG, Landmark B, Kirkehei I, Reinar LM. **Effekt av langtids mekanisk ventilering (LTMV) del 1 - nevromuskulær sykdom eller svikt i sentral respirasjonsstyring**. Oslo: Nasjonalt kunnskapssenter for helsetjenesten, 2012. (Rapport fra Kunnskapssenteret nr 13-2012.)	Bakgrunn: Langtids mekanisk ventilering (LTMV) skal bidra til å opprettholde tilfredsstillende åndedrett gjennom kortere eller lengre perioder. Pasienter som har behov for LTMV gjennom hele eller deler av døgnet er an mangeartet gruppe med hensyn til alder og diagnoser. Norske registerdata viser store regionale forskjeller i hvilke kriterier som legges til grunn for oppstart av behandling med LTMV. Oppdrag: Helsedirektoratet har bedt Kunnskapssenteret om å utarbeide en systematisk oversikt om effekt av LTMV. Som svar på bestillingen publiserer vi en rapportserie bestående av tre delrapporter. I denne første delrapporten oppsummerer vi forskning om effekt av LTMV for pasienter med nevromuskulære lidelser og for pasienter med svikt i sentral respirasjonsstyring. Hovedfunn: • LTMV kan føre til en viss livsforlengelse og bedre livskvalitet for pasienter med amyotrofisk lateralsklerose (ALS), og effekten er muligens størst for pasienter med god tale-, tygge- og svelgefunksjon. Dokumentasjonen er av lav kvalitet. Det er derfor vanskelig å trekke sikre konklusjoner basert på forskningen alene. • LTMV kan føre til livsforlengelse for underventilerte pasienter med Duchennes muskeldystrofi. Dokumentasjonen er av lav kvalitet, og det er derfor vanskelig å trekke sikre konklusjoner basert på forskningen alene. • Uavhengig av diagnose kan oppstart av LTMV assosieres med nedgang i antall sykehusinnleggelser. LTMV med invasiv tilslutning kan muligens assosieres med større risiko for komplikasjoner og sykehusinnleggelser enn ikke-invasiv LTMV, det vil si maskebehandling. Dokumentasjonen er av svært lav kvalitet, som betyr at det ikke er mulig å trekke sikre konklusjoner. • For noen aktuelle diagnoser, herunder svikt i sentral respirasjonsstyring, finnes det svært lite forskning om effekt av LTMV.
8.	McKim DA, Road J, Avendano M, Abdool S, Cote F, Duguid N, et al. **Home mechanical ventilation: A Canadian Thoracic Society clinical practice**	Sammendrag: Increasing numbers of patients are surviving episodes of prolonged mechanical ventilation or benefitting from the recent availability of userfriendly noninvasive ventilators. Although many publications pertaining to specific aspects of home mechanical ventilation (HMV) exist, very few comprehensive guidelines that bring together all of the current literature on patients at risk for or using mechanical ventilatory support are available. The Canadian Thoracic Society HMV Guideline Committee has reviewed the available English literature on topics related to HMV in adults, and completed a detailed guideline that will help standardize and improve the assessment and management of individuals requiring noninvasive or invasive HMV. The guideline

	guideline. Canadian Respiratory Journal 2011;18(4):197-215.	provides a disease-specific review of illnesses including amyotrophic lateral sclerosis, spinal cord injury, muscular dystrophies, myotonic dystrophy, kyphoscoliosis, post-polio syndrome, central hypoventilation syndrome, obesity hypoventilation syndrome, and chronic obstructive pulmonary disease as well as important common themes such as airway clearance and the process of transition to home. The guidelines have been extensively reviewed by international experts, allied health professionals and target audiences. They will be updated on a regular basis to incorporate any new information.
9.	Radunovic A, Annane D, Jewitt K, Mustfa N. **Mechanical ventilation for amyotrophic lateral sclerosis/motor neuron disease**. Sao Paulo Medical Journal 2010;128(2):108-109.	BACKGROUND: Amyotrophic lateral sclerosis, also known as motor neuron disease, is a fatal neurodegenerative disease. Without mechanical ventilation, death from respiratory failure usually follows within two to five years of the onset of symptoms. OBJECTIVES: To examine the efficacy of mechanical ventilation (tracheostomy and non-invasive ventilation) in improving survival, on disease progression and quality of life in amyotrophic lateral sclerosis. SEARCH STRATEGY: We searched The Cochrane Neuromuscular Disease Group Trials Specialized Register (December 8 2008), The Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 4, 2008), MEDLINE (January 1966 to December 2008), EMBASE (January 1947 to December 2008), CINAHL Plus (January 1937 to December 2008), and AMED (January 1985 to December 2008). We also searched for ongoing studies on clinicaltrials.gov. SELECTION CRITERIA: Randomised and quasi-randomised controlled trials involving non-invasive or tracheostomy assisted ventilation in participants with a clinical diagnosis of amyotrophic lateral sclerosis. DATA COLLECTION AND ANALYSIS: Four authors independently selected studies for assessment. All authors extracted data independently from the full text of selected studies and assessed the risk of bias in studies that met the inclusion criteria. We attempted to obtain missing data where possible. MAIN RESULTS: Two randomised controlled trials involving 54 participants receiving non-invasive ventilation were identified and included. Incomplete data were published for one study and we contacted the trial authors who were not able to provide the missing data. Therefore the results of the review were based on a single study of 41 participants. The study showed that the overall median survival in the whole cohort after initiation of assisted ventilation was significantly different between the non-invasive ventilation and standard care groups (P = 0.0062) with a median survival for the non-invasive ventilation group patients of 48 days longer than the standard care group participants. Non-invasive ventilation significantly improved survival and quality of life in the subgroup with normal to moderately impaired bulbar function. Non-invasive ventilation did not prolong survival in patients with poor bulbar function although it showed significant improvement in the mean symptoms domain of the sleep apnoea quality-of-life index but not in the Short Form-36 quality of life mental component summary score. AUTHORS' CONCLUSIONS: Evidence from a single randomised trial of non-

		invasive ventilation in 41 participants suggests that it significantly prolongs survival and improves or maintains quality of life in people with ALS. Survival and some measures of quality of life were significantly improved in the subgroup of people with better bulbar function, but not in those with severe bulbar impairment.
10.	Bausewein C, Booth S, Gysels M, Higginson I. **Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases**. Cochrane Database of Systematic Reviews 2008(2):CD005623.	Background: Breathlessness is a common and distressing symptom in the advanced stages of malignant and non-malignant diseases. Appropriate management requires both pharmacological and non-pharmacological interventions. Objectives: The primary objective was to determine the effectiveness of non-pharmacological and non-invasive interventions to relieve breathlessness in participants suffering from the five most common conditions causing breathlessness in advanced disease. Search strategy: We searched the following databases: The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, British Nursing Index, PsycINFO, Science Citation Index Expanded, AMED, The Cochrane Pain, Palliative and Supportive Care Trials Register, The Cochrane Database of Systematic Reviews, and Database of Abstracts of Reviews of Effectiveness in June 2007. We also searched various websites and reference lists of relevant articles and textbooks. Selection criteria: We included randomised controlled and controlled clinical trials assessing the effects of non-pharmacological and non-invasive interventions to relieve breathlessness in participants described as suffering from breathlessness due to advanced stages of cancer, chronic obstructive pulmonary disease (COPD), interstitial lung disease, chronic heart failure or motor neurone disease. Data collection and analysis: Two review authors independently assessed relevant studies for inclusion. Data extraction and quality assessment was performed by three review authors and checked by two other review authors. Meta-analysis was not attempted due to heterogeneity of studies. Main results: Forty-seven studies were included (2532 participants) and categorised as follows: single component interventions with subcategories of walking aids (n = 7), distractive auditory stimuli (music) (n = 6), chest wall vibration (CWV, n = 5), acupuncture/acupressure (n = 5), relaxation (n = 4), neuro-electricalmuscle stimulation (NMES, n = 3) and fan (n = 2). Multi-component interventions were categorised in to counselling and support (n = 5), breathing training (n = 3), counselling and support with breathing-relaxation training (n = 2), case management (n = 2) and psychotherapy (n = 2). There was a high strength of evidence that NMES and CWV could relieve breathlessness and moderate strength for the use of walking aids and breathing training. There is a low strength of evidence that acupuncture/acupressure is helpful. There is not enough data to judge the evidence for distractive auditory stimuli (music), relaxation, fan, counselling and support, counselling and support with breathing-relaxation training, case management and psychotherapy. Most studies have been conducted in COPD patients, only a few studies included participants with other conditions. Authors' conclusions: Breathing training, walking aids, NMES and CWV appear to be effective non-pharmacological interventions for relieving breathlessness in advanced stages of disease.

11.	**Diaphragmatic Stimulators for Amyotrophic Lateral Sclerosis Patients: Clinical Effectiveness** Canadian Agency for Drugs and Technology in Health; 2008.	Sammendrag ikke tilgjengelig.
12.	Piepers S, van den Berg JP, Kalmijn S, van der Pol WL, Wokke JH, Lindeman E, et al. **Effect of non-invasive ventilation on survival, quality of life, respiratory function and cognition: a review of the literature**. Amyotrophic Lateral Sclerosise 2006;7(4):195-200.	Symptoms of nocturnal hypoventilation may negatively influence the quality of life (QoL) of ALS patients long before respiratory failure ensues. Non-invasive mechanical ventilation (NIV) is considered a treatment option for nocturnal hypoventilation. The primary objective of NIV is improving quality of life (QoL). It may also prolong life by several months. A systematic review of the literature was performed to analyse what is known of the effect of NIV on survival, QoL and other outcome measures. A computerized literature search was performed to identify controlled clinical trials and observational studies of treatment of ALS-associated nocturnal hypoventilation from 1985 until May 2005. Twelve studies fulfilled the inclusion criteria. Four studies were retrospective, seven prospective and in one study randomization was used. All studies reported beneficial effects of NIV on all outcome measures. In seven studies NIV was associated with prolonged survival in patients tolerant for NIV, and five studies reported an improved QoL. In conclusion, studies on the use of NIV in ALS differ in study design and endpoint definitions. All studies suggest a beneficial effect on QoL and other outcome measures (Evidence level Class II-III). Well-designed randomized controlled trials comparing the effect on QoL and survival have not been performed.
13.	Heffernan C, Jenkinson C, Holmes T, Macleod H, Kinnear W, Oliver D, et al. **Management of respiration in MND/ALS patients: an evidence based review**. Amyotrophic Lateral Sclerosise 2006;7(1):5-15.	This systematic review comprises an objective appraisal of the evidence in regard to the management of respiration in patients with motor neuron disease (MND/ALS). Studies were identified through computerised searches of 32 databases. Internet searches of websites of drug companies and MND/ALS research web sites, 'snow balling' and hand searches were also employed to locate any unpublished study or other 'grey literature' on respiration and MND/ALS. Since management of MND/ALS involves a number of health professionals and care workers, searches were made across multiple disciplines. No time frame was imposed on the search in order to increase the probability of identifying all relevant studies, although there was a final limit of March 2005. Recommendations for patient and carer-based guidelines for the clinical management of respiration for MND/ALS patients are suggested on the basis of qualitative analyses of the available evidence. However, these

		recommendations are based on current evidence of best practice, which largely comprises observational research and clinical opinion. There is a clear need for further evidence, in particular randomised and non-randomised controlled trials on the effects of non-invasive ventilation and additional larger scale cohort studies on the issues of initial assessment of respiratory symptoms, and management and timing of interventions.
14.	Eng D. **Management guidelines for motor neurone disease patients on non-invasive ventilation at home**. Palliative Medicine 2006;20(2):69-79.	Most motor neurone disease (MND) patients die of respiratory system complications. When patients have advanced disease with symptoms of respiratory failure, management issues can become complicated by the introduction of assisted ventilatory devices. Therefore, care provision by a multidisciplinary team must be structured and co-ordinated in order to ensure that patients and their carers receive the optimal level of care. The objective of this article is to review the literature and explore the complex issues surrounding the use of non-invasive positive pressure ventilation (NIPPV) in home care MND patients as a justification for the development of a management guideline for medical practitioners. A guideline for multidisciplinary care of home ventilated MND patients will be proposed.

Opplevelser og erfaringer (kvalitativ forskning)

Tab. 19: Systematiske oversikter om pasienter og pårørendes opplevelser og erfaringer

	Referanse	Sammendrag
1.	Soundy A, Condon N. **Patients experiences of maintaining mental well-being and hope within motor neuron disease: a thematic synthesis**. Frontiers in Psychology 2015;6:606.	Research is required that can synthesize the experiences of patients with Motor Neuron Disease (MND). One value of being able to do this is to understand the psychological experiences and processes involved in maintaining mental well-being and hope. A qualitative thematic synthesis of studies was undertaken. Studies were electronically searched from inception until June 2014. Twenty-nine studies with 342 (175 male) unique individuals with MND were identified. Five themes were identified: (1)The effects of the disease on interactions, relationships, roles and meaningful activities, (2) Responses that relate to the expression of hope, (3) Factors which disable hope, (4) Factors which enable hope, and (5) Cognitive and Practical adaptation that enabled hope, control and coping. Finally, a model of hope enablement was identified that considers the psychological pathways undertaken by a patient which influence mental well-being and hope. Within this review article evidence is provided which illustrates the central importance of relationships and social support for individuals with MND. Further, it has been identified that periods of coping are possible and are likely associated with greater mental well-being for patients with MND.

2.	Connolly S, Galvin M, Hardiman O. **End of life in patients with amyotrophic lateral sclerosis (ALS): A review**. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 2014;15:118.	Background: ALS is an incurable condition with approximately 70% of those affected dying within three years from symptom onset. However, there has been relatively little discussion about the end-of-life phase; perhaps because the thrust of medical education is generally towards curative therapies and end-of-life discussions require a different perspective, including coming to terms with the limitations of medical interventions as life promoting initiatives. Objectives: The aim of this review is to identify and review the most important themes in the context of management of end of life in ALS. Methods: Relevant end-of-life themes were identified by a literature search and through discussion with health professionals in Neurology and Palliative Care in the Irish National Centre for ALS. Relevant publications were identified through a search of Medline and Pubmed using the following Keywords: motor neuron disease (MND), amyotrophic lateral sclerosis (ALS), end of life, dying, death, decision-making, advance care directive and euthanasia. Results: Through discussion with health professionals and literature search five major themes were identified - (1) importance of end-of-life discussions and decisions; (2) use of life prolonging interventions and technologies; (3) life limiting interventions (4) the experience of dying and (5) best practice at end of life. Discussion and conclusion: Early and honest discussion of end-of-life issues allows time for reflection and planning, can obviate the introduction of unwanted interventions or procedures, and help alleviate fear around dying. Advance care directives can provide patients with options to exercize autonomy regarding preferred end-of-life management strategies, although their legal validity and use varies from country to country. Preferences around end-of-life interventions and use of technologies vary, and it is important that health care professionals respect patients autonomy. Formal care at the end of life should aim to maximize quality of life of both the patient and caregiver and where possible incorporate appropriate palliation of distressing physical, psychosocial and existential distress. Training of health care professionals should include the development of skills that help to sensitively manage the inevitability of death in terminal illnesses such as ALS. While the importance of end-of-life care is increasingly being recognized, the particular needs of ALS patients and their families require more attention. Successful management of patients through the end-of-life period can be challenging for the healthcare professional, trained in promoting life and preventing death.
3.	Aoun SM, Bentley B, Funk L, Toye C, Grande G, Stajduhar KJ. **A 10-year literature review of family caregiving for motor neurone disease: moving from caregiver burden studies to**	BACKGROUND: There is growing awareness that different terminal diseases translate into different family caregiver experiences, and the palliative and supportive care needs of these families are both similar and unique. Family members caring for people with motor neurone disease may experience exceptional strain due to the usually rapid and progressive nature of this terminal illness. AIM: The purpose of this review is to synthesize contemporary research and provide a comprehensive summary of findings relevant to motor neurone disease family caregivers, as well as highlight some of the suggested interventions to alleviate burden and improve quality of life for this group. DESIGN: We conducted a comprehensive review of empirical research on family caregiving for people with motor neurone disease in peer-reviewed journals published in English, January 2000-April 2011. Fifty-nine studies met the inclusion criteria.

	palliative care interventions. Palliative Medicine 2013;27(5):437-446.	RESULTS: This comprehensive literature review was consistent with previous research documenting the substantial burden and distress experienced by motor neurone disease family caregivers and revealed important points in the trajectory of care that have the potential for negative effects. The diagnosis experience, assisted ventilation, cognitive changes and end-of-life decision making create challenges within a short time. This review has also implicated the need for improvements in access to palliative care services and highlighted the absence of interventions to improve care. CONCLUSIONS: Caregiver burden and quality-of-life studies on motor neurone disease family caregivers have so far dominated the research landscape .The focus needs to be on developing interventions that provide direct practical and psychosocial supports for motor neurone disease family caregivers.
4.	Sakellariou D, Boniface G, Brown P. **Experiences of living with motor neurone disease: a review of qualitative research**. Disability & Rehabilitation 2013;35(21):1765-1773.	Purpose: This review sought to answer the question 'what is known about people's experiences of living with MND?'. Methods: The review followed the guidelines of the Centre of Reviews and Dissemination. Twenty articles met the inclusion criteria and their results were analysed thematically. Data were managed and coded using the software package NVIVO and the analysis was performed in two stages, with the first stage aiming to develop descriptive themes offering an overview of the included data. During the second stage, analytical themes were developed with the explicit aim to answer the review question. Results: The themes that emerged point to the following: (a) people with motor neurone disease (MND) develop experiential knowledge that helps them to live with the disease and (b) while people with MND believe they do not have any control over the disease, they try to have control over their lives through active choices, e.g. how and when to use adaptive equipment. Conclusions: This review highlights the decision-making and knowledge generating processes used by people with MND. Further research is required to explore these processes and their implications for the care of people with MND.
5.	O'Brien MR, Clark D. **Spirituality and faith: Means for coping with the effects of motor neurone disease (MND)**. Palliative Medicine 2012;26 (4):500-501.	Aims: To explore the personal experience of living with MND as documented in personal illness narratives, written by people diagnosed with the illness and examine the role of spirituality and faith as means of coping with the illness. Methods: A systematic search strategy was used to identify and locate published and unpublished personal illness narratives written by people diagnosed with MND. Content and thematic analysis was aided by Nvivo 7 software. Results: First-person accounts of living with MND written from 1986-2005, by 161 individuals, were obtained. Throughout the narratives there is frequent reference to the power of spirituality to impact positively on the illness experience. People refer to the strength acquired from seeking a spiritual understanding of their circumstances. There is a sense of being used for a 'higher purpose', being seen as a spiritual example to others. Religious convictions are frequently strengthened following the diagnosis and are sustained by a conviction that 'God' will not burden them beyond their ability to cope. Faith is regarded, by some, as a cornerstone in coming to terms with their future. Belief in an afterlife sustains many authors as they recognise the present time as just a small part of a much longer time span. Conclusions: It is evident within the narratives that people with MND tolerate distress through maintaining hope by belief in a divine

		entity and through connection with a higher being or with other people, which reflects the importance of relational values in coping with MND. Seeking answers to life's questions at an existential level enables many individuals to sustain hope and arrive at a sense of peace with their situation. Spirituality should be regarded as an important resource for coping with MND.
6.	Hubbard G, McLachlan K, Forbat L, Munday D. **Recognition by family members that relatives with neurodegenerative disease are likely to die within a year: a meta-ethnography**. Palliative Medicine 2012;26(2):108-122.	OBJECTIVE: To synthesize evidence of family members recognizing that their relative is likely to die within the year, and identifying the need for palliative care. DESIGN: A meta-ethnography of studies of family members in multiple sclerosis (MS), Parkinson's disease (PD) and motor neuron disease (MND). REVIEW METHODS: Systematic search in electronic databases; thematic synthesis guided by the principles of meta-ethnography, which is a method for thematic synthesis of qualitative studies. RESULTS: Nine articles were included. The results of the synthesis identified two key themes. First, family members are intimately aware of changes in their relative's health and well-being. Sub-themes include family member awareness of different and progressive stages of the disease, noticing deterioration, noticing decline in functional abilities and recognizing that their relative will die. The second key theme is dilemmas of being involved in prognostication. Sub-themes include family member ambivalence toward hearing about prognostication, health professionals not being knowledgeable of the disease and family reluctance to receive palliative care. CONCLUSIONS: Family members monitor and recognize changes in their relative with PD, MND and MS and in themselves. Thus, drawing on the expertise of family members may be a useful tool for prognostication.
7.	Foley G, Timonen V, Hardiman O. **Patients' perceptions of services and preferences for care in amyotrophic lateral sclerosis: a review**. Amyotrophic Lateral Sclerosis 2012;13(1):11-24.	Service providers and service users often have different perspectives on health and social care services. We have undertaken a systematic review of empirical data between 1988 and March 2011 relating to ALS service users' perspectives on health and social care services. Forty-seven texts were extracted and a narrative synthesis conducted. Few studies have explored ALS patients' experiences in relation to their satisfaction with services. Our review showed that ALS patients expect dignified care but they are often dissatisfied with health care services and have unmet expectations of their care. Most studies of decision-making and preferences for care have focused on end-of-life intervention. Various factors influence preferences for care from the service user perspective and people with ALS may adjust their use of services as they negotiate change. In conclusion, further research on the timeliness of services to meet changing needs of service users is required. The service user experience of allied health care services prior to end-of-life care also warrants investigation. Service providers need to support people with ALS as they negotiate feelings of acceptance and independence. Research to identify the key parameters of the ALS patient experience of services is required.

8.	Seeber AA, Hijdra A, Vermeulen M, Willems DL. **Discussions about treatment restrictions in chronic neurologic diseases: a structured review**. Neurology 2012;78(8):590-597.	OBJECTIVE: Many incurable neurologic diseases have predictable complications during their course or at their end stage. Timely discussions of potential treatment restrictions may improve the quality of treatment decisions toward the end of life. What is known about the actual practice of these discussions? METHODS: We performed a literature search in MEDLINE, EMBASE, and CINAHL for empirical studies about discussions and decisions to restrict treatment in the course of 6 conditions: motor neuron disease (amyotrophic lateral sclerosis [ALS]), primary malignant brain tumors, multiple sclerosis, stroke, Parkinson disease, and dementia (Alzheimer disease). RESULTS: In 10 of 43 studies, the actual practice of decision-making was studied; in the remaining 33, caregivers were interviewed about this practice. Three scenarios were described: 1) acute devastating disease (severe stroke); 2) stable severe neurologic deficit with complications (poststroke brain damage); and 3) chronic progressive disease with complications (dementia and ALS). We found no studies concerning the other conditions. In all 3 scenarios, discussions and decisions seemed to be mostly triggered by the occurrence of life-threatening situations, either caused by the disease itself (1), or complications (2 and 3, including many patients with ALS). Some ALS studies showed that timely discussion of treatment options improved end-of-life decision-making. CONCLUSIONS: The actual practice of discussions about treatment restrictions in chronic neurologic disease has hardly been studied. The currently available empirical data suggest that discussions are mainly triggered by life-threatening situations, whereas anticipation of such situations may be beneficial for patients and their families.
9.	Foley G, Timonen V, Hardiman O. **A systematic review of als service users ' Perceptions of services and decision making in care**. Amyotrophic Lateral Sclerosis 2011;12:13.	Background: Effective symptom management, physical and psychological support, are components of ALS care.Service users and providers of palliative services can hold different perspectives on the benefits of care.However, few studies have explored the delivery of services from the ALS service user's perspective. Objectives: To examine the literature on ALS service users ' perceptions of health care services; to draw attention to factors that may influence preferences for care.Method: A review of the literature from 1988 to March 2011 was undertaken .Databases used included; Medline, Cinahl, AMED, PsycInfo, Cochrane Library, Evidence Based Medicine Reviews, Science Citation Index, Social Sciences Citation Index, and Arts and Humanities Citation Index.Search terms used included; ' amyotrophic lateral sclerosis ' or ' motor neurone disease ' and/or ' services ' , ' healthcare ' , ' experiences ' , ' expectations ' , ' satisfaction ' , ' decision-making ' , ' perceptions ' , ' perspectives ' and ' care preferences ' .Separate manual searches of online editions of palliative care journals (including early online where available) were also undertaken using search terms ' motor neurone disease ' and ' amyotrophic lateral sclerosis ' .A narrative approach was used to synthesise studies (1). Results: Studies of decision making and preferences for care have focussed primarily on end-of-life intervention.Only few studies report on service users ' decision making in services prior to end-of-life care. According to existing literature, dissatisfaction with services relates to absence of specialised care; limited access to assistive devices; inadequate respite care and emotional support; delays in diagnosis; concerns regarding method of disclosure; and a lack of knowledge about ALS among professionals.Satisfaction with services is confined primarily to the use of assistive devices.Service users also seek autonomy and exert control when making decisions about care.The need to exert control remains stable overtime.However, care preferences change

		to accommodate to evolving perspectives and support systems.Discussion: The literature suggests that ALS service users expect dignified care but they have unmet expectations of their care. A combination of personal values, desire to maintain control, perceptions about quality life, social and carer support determine service users ' preferences for and decisions about care.Some service users may resign themselves to the inevitability of ALS.However, the majority seek a broad range of services and some maintain positive perceptions about health.Conclusion: ALS service users make choices about care that are grounded in how they interpret their own lives and how they judge potential benefits of care.
10.	Taminiau-Bloem EF, Visser MR, Tishelman C, Koeneman MA, van Zuuren FJ, Sprangers MA. **Somatically ill persons' self-nominated quality of life domains: review of the literature and guidelines for future studies**. Quality of Life Research 2010;19(2):253-291.	OBJECTIVE: To review which domains somatically ill persons nominate as constituting their QoL. Specific objective is to examine whether the method of enquiry affect these domains. METHODS: We conducted two literature searches in the databases PubMed/Medline, CINAHL and Psychinfo for qualitative studies examining patients' self-defined QoL domains using (1) SEIQoL and (2) study-specific questions. For each database, two researchers independently assessed the eligibility of the retrieved abstracts and three researchers subsequently classified all QoL domains. RESULTS: Thirty-six eligible papers were identified: 27 studies using the SEIQoL, and nine presenting data derived from study-specific questions. The influence of the method of enquiry on patients' self-nominated QoL domains appears limited: most domains were presented in both types of studies, albeit with different frequencies. CONCLUSIONS: This review provides a comprehensive overview of somatically ill persons' self-nominated QoL domains. However, limitations inherent to reviewing qualitative studies (e.g., the varying level of abstraction of patients' self-defined QoL domains), limitations of the included studies and limitations inherent to the review process, hinder cross-study comparisons. Therefore, we provide guidelines to address shortcomings of qualitative reports amenable to improvement and to stimulate further improvement of conducting and reporting qualitative research aimed at exploring respondents' self-nominated QoL domains.Copyright © The Author(s) 2010. This article is published with open access at Springerlink.com
11.	Williams AL. **Perspectives on spirituality at the end of life: a meta-summary**. Palliative & Supportive Care 2006;4(4):407-417.	OBJECTIVE: A meta-summary of the qualitative literature on spiritual perspectives of adults who are at the end of life was undertaken to summarily analyze the research to date and identify areas for future research on the relationship of spirituality with physical, functional, and psychosocial outcomes in the health care setting. METHODS: Included were all English language reports from 1966 to the present catalogued in PubMed, Medline, PsycInfo, and CINAHL, identifiable as qualitative investigations of the spiritual perspectives of adults at the end of life. The final sample includes 11 articles, collectively representing data from 217 adults. RESULTS: The preponderance of participants had a diagnosis of cancer; those with HIV/AIDS, cardiovascular disease, and ALS were also represented. Approximately half the studies were conducted in the United States; others were performed in Australia, Finland, Scotland, and Taiwan. Following a process of theme extraction and abstraction, thematic patterns emerged and effect

		sizes were calculated. A spectrum of spirituality at the end of life encompassing spiritual despair (alienation, loss of self, dissonance), spiritual work (forgiveness, self-exploration, search for balance), and spiritual well-being (connection, self-actualization, consonance) emerged. SIGNIFICANCE: The findings from this meta-summary confirm the fundamental importance of spirituality at the end of life and highlight the shifts in spiritual health that are possible when a terminally ill person is able to do the necessary spiritual work. Existing end-of-life frameworks neglect spiritual work and consequently may be deficient in guiding research. The area of spiritual work is fertile ground for further investigation, especially interventions aimed at improving spiritual health and general quality of life among the dying.

Livskvalitet

Tab. 20: Systematiske oversikter om sammenhengen mellom ulike faktorer og livskvalitet

	Referanse	Sammendrag
1.	Young C, Aynsley G. **ALS symptoms, disability and quality of life : Literature review and model generation**. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 2014;15:108-109.	Background: The limited efficacy of disease modifiers for ALS/MND focuses management on symptom control and maintaining quality of life (QoL). As yet, there is no overview of how different symptoms may influence QoL in ALS/MND and how all the possible factors interplay. We conducted a systematic literature review to determine how symptoms influence QoL for people with ALS/MND, in preparation for the Trajectories of Outcome in Neurological Conditions (TONiC) study, a British multicentre study of QoL in MND. Objectives: This study reviews the published evidence on symptoms influencing QoL, identifying potential direct and indirect effects. Methods: Literature searches were conducted in PubMed, Science Direct, Science Citation Index, EBSCOHOST, Scopus, CINAHL and PsycInfo to identify primary studies published from 1999 to March 2014 inclusive, assessing how disability or symptoms affect QoL in ALS/MND. The symptom list was derived from the American Academy of Neurology ALS Practice Parameters (1). Studies were excluded if their aim was to evaluate the effect of a therapy on QoL or if they provided no data on correlation between symptom and QoL. Direct effects were determined by correlation coefficients, graded according to standard statistical criteria (2). Indirect effects were factors correlating with a direct effect. Results: 111 potential studies were identified; of these, 82 met exclusion criteria. This left 29 studies describing overall disability severity and 7 symptoms as show-

		ing correlations with QoL. In descending order of strength of correlation coefficients, these were overall disability severity, dyspnoea, fatigue, cognitive impairment, depression, emotional lability, anxiety and muscle weakness. Data on every factor for which more than one study was available was conflicting, in that there was at least one study showing no correlation as well as one or more showing some correlation. Factors indirectly contributing were pain (through low mood, anxiety, overall disability severity) and poor sleep (through dyspnoea and fatigue.) There were no studies providing information on correlations between cramps, sialorrhoea, spasticity, dysphagia or weight loss with QoL. A potential multifactorial model of symptoms influencing QoL directly and indirectly has been developed. Discussion and conclusion: There is preliminary evidence that several physical and psychological symptoms do directly impact QoL for people with ALS/MND. Comparison of studies was challenging due to heterogeneity in study design and outcome measures. Inconsistencies between studies may reflect methodological variations. Some factors appear to have indirect effects by mediating other factors. Further work is needed to systematically identify potential factors and test these in large studies capable of examining direct and indirect effects.
2.	Nee L, Goldstein L, Young C. **Psychosocial factors affecting quality of life in motor neurone disease: A systematic review of the literature**. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 2013;14:74-75.	Background: As motor neurone disease (MND/ALS) is progressive and fatal, supporting quality of life (QOL) is a primary concern. Previous work has found QOL in MND/ ALS to be weakly related to physical dysfunction, whereas some psychosocial factors appeared important. Objective: To conduct a systematic literature review to determine psychosocial factors affecting QOL in MND/ALS, in preparation for the Trajectories of Outcome in Neurological Conditions (TONiC) study, a multicentre national study of QOL in MND/ALS. Methods: Literature searches were conducted in Medline, Psychinfo, Cochrane Library, and the Amyotrophic Lateral Sclerosis and Frontotemporal Dementia journal to identify studies reporting relationships between psychosocial factors and QOL in people with MND/ALS. Results: One hundred and three potential studies were retrieved after assessing the abstracts of publications identified through the searches. Of these, 75 were omitted on the basis of exclusion criteria such as reviews, case studies, diseases other than MND/ALS, outcomes other than QOL, psychosocial factors not included, and not published in English. This left 28 studies meeting the eligibility criteria. Five psychosocial factors were identified: These were social support; affective state (depression, anxiety, and hopelessness); religion/spirituality; coping strategies; and personality traits. Fifteen studies reported a positive relationship between social support and QOL. There were discrepancies among studies investigating affective state. Eight studies found that depression was negatively associated with QOL, whereas six found no significant relationship. Likewise, findings on anxiety were inconsistent. Four studies reported a negative association between anxiety and QOL while three found no relationship. Only two studies investigated hopelessness and in both it was negatively associated with QOL. While religion/ spirituality was a positive factor in eight studies, one study disputed this. Coping strategies (two studies) and personality traits (two studies) received limited attention. Discussion and conclusion: Social support has the strongest and most consistent evidence as a factor associated with QOL in MND/ALS. Discrepancies in the literature on affective state may be attributable to methodological considerations, such as differences in how QOL is conceptualised or measured. Fewer studies investigated anxiety than depression, despite several studies finding anxiety to be more strongly associated than depression with QOL. Anxiety may therefore represent an underestimated problem. Future research should establish its role. While the potential influence

		of religion/ spirituality on QOL is strongly supported in the literature, one study found that patients infrequently identified it as a relevant factor. That study was conducted in a secularised country (Sweden). Future research should establish whether religion/spirituality is an important factor across different populations of MND/ALS patients. Coping strategies and personality traits warrant additional investigation. Of further note, all reviewed studies were observational. Interventional designs are required to investigate whether interventions targeting psychosocial factors positively affect QOL.
3.	Mohammad M, Young C. **Bulbar symptoms as physical determinants of quality of life in patients with amyotrophic lateral sclerosis: A systematic review**. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 2013;14:73-74.	Background: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease which can cause bulbar symptoms such as dysarthria, dysphagia and sialorrhoea. Previous work has found quality of life (QOL) in ALS to be weakly related to physical dysfunction and psychosocial factors appeared more influential. However, bulbar symptoms may be very distressing to people with ALS and so it is important to explore how these symptoms may affect QOL. Objective: To systematically review existing literature concerning the effects of dysarthria, dysphagia or sialorrhoea on the QOL of patients with ALS, in preparation for the Trajectories of Outcome in Neurological Conditions (TONiC) study, a multicentre national study of QOL in ALS. Methods: MEDLINE (1990 - 2013), ScienceDirect (1990 - 2013), Ovid SP (1990 - 2013) and Compendex (1990 - 2013) were searched. Inclusion criteria stated studies must examine one of the three symptoms and have QOL as an outcome measure. The bibliographies of other studies which examined physical and psychological determinants of QOL in ALS were reviewed for additional references. Results: For dysarthria, there were one non-blind experimental and one prospective study. In both studies, QOL was assessed in relation to communication support. Both concluded that there was a significant improvement in QOL with the introduction of communication support. Dysarthria was the only factor looked at in relation to QOL in the experimental study, but the prospective study also looked at non-invasive ventilation methods. For dysphagia, one survey was found on swallowing function. It concluded that apart from nutritional deficiencies created by dysphagia, there was also a reduction in QOL. For sialorrhoea, one double-blind randomized trial and five open-label prospective studies were found. The randomized trial showed no significant improvement in QOL after botulinum toxin treatment. From the five open-label studies, four looked at botulinum treatment and one looked at radiotherapy. All open-label studies concluded an effect on QOL. Discussion and conclusion: The studies in this systematic review show variations in the methods used for measuring QOL, which impairs comparison between studies, and may have influenced findings. Each study has a small sample size which weakens the validity of their conclusions but as a group of nine studies, eight concluded that there was a relationship between QOL and bulbar symptoms. Physical, specifically bulbar, symptoms are associated with QOL in ALS. This highlights the possibility that psychosocial symptoms could be confounding physical symptoms when both are examined in combination. Further research is needed into the physical determinants of QOL, including looking at bulbar symptoms as they have been shown to have an impact on QOL in these initial studies.

Økonomi

Tab. 21: Systematiske oversikter om kostnader

	Referanse	Sammendrag
1.	Gladman M, Zinman L. **The economic impact of amyotrophic lateral sclerosis: a systematic review**. Expert Review of Pharmacoeconomics & Outcomes Research 2015;15(3):439-450.	Amyotrophic lateral sclerosis (ALS) is a devastating neurological disease for which there is no cure, and the associated economic burden is considerable. In this review, the authors summarize the existing body of literature pertaining to the costs associated with ALS to demonstrate the scale and scope of the economic burden of this paralyzing disease. Twelve studies from eight countries published between January 2001 and January 2015 met the inclusion criteria and were included in this review. Direct and indirect costs varied significantly across countries. Standardized to the 2015 US$, the annual total cost per patient ranged from US$ 13,667 in Denmark to as high as US$ 69,475 in the USA, with the national economic burden of ALS estimated at US$ 279-472 million in the USA. Costs associated with ALS were greater than that of other neurological diseases, indicating a continued need for medical advances and financial support for patients and families. Regional cost analyses are necessary to determine how best to spend funds that have been raised globally from the ice bucket phenomenon.
2.	Costa N, Deruemaux-Burel H, Molinier L. **What are indirect costs in neurodegenerative diseases? a methodological review**. Value in Health 2014;17 (3):A186.	Objectives: Neurodegenerative diseases (NDs) refer to a group of diseases that affect brain cells. Alzheimer disease (AD), Parkinson disease (PD), Amyotrophique Lateral Sclerosis (ALS) and Multiple Sclerosis (MS) are the most prevalent NDs. NDs cause a substantial economic burden worldwide and indirect costs are an important component of total costs. This study aims to review relevant papers to characterize the different components of indirect costs and to identify the weight of indirect costs on total costs in different NDs. Methods: A systematic bibliographic search was performed on an international medical literature database (MEDLINE). All studies which assessed the social economic burden and indirect costs of different NDs were selected. Indirect costs were characterized into several types (i.e. sick leave, presenteeism, early retirement, premature death, reduction in working hours, informal care time) and into several valuation (i.e. Human Capital Approach, Friction Cost Method, Willingness To Pay). Results: 44 studies met our criteria. Depending on studies, the percentage of indirect costs on total costs varies from 1% to 68% in PD, from 2% to 89% in AD, from 24% to 59% in ALS and from 29% to 78% in MS. The main indirect costs component was early retirement in PD, ALS and MS. This component varies from 61% to 95% of indirect costs in PD, from 35% to 88% in ALS and from 61% to 95% in MS. The main indirect costs component in AD was informal care time and account for almost 100% of indirect costs. Indirect costs increase with severity level in AD and MS, and decrease with severity level in ALS. Conclusions: Components of indirect costs are different depending on studies and especially for AD where indirect costs mainly refer to informal costs which should be considered as a full cost category to avoid the lack of understanding.

Etikk

Tab. 22: Systematisk oversikt over studier på etikk

	Referanse	Sammendrag
1.	Seitzer F, Kahrass H, Neitzke G, Strech D. **The full spectrum of ethical issues in the care of patients with ALS: a systematic qualitative review**. J Neurol 2015.	Dealing systematically with ethical issues in amyotrophic lateral sclerosis (ALS) care requires an unbiased awareness of all the relevant ethical issues. The aim of the study was to determine systematically and transparently the full spectrum of ethical issues in ALS care. We conducted a systematic review in Medline and Google Books (restricted to English and German literature published between 1993 and 2014). We applied qualitative text analysis and normative analysis to categorise the spectrum of ethical issues in ALS care. The literature review retrieved 56 references that together mentioned a spectrum of 103 ethical issues in ALS care. The spectrum was structured into six major categories that consist of first and second-order categories of ethical issues. The systematically derived spectrum of ethical issues in ALS care presented in this paper raises awareness and understanding of the complexity of ethical issues in ALS care. It also offers a basis for the systematic development of informational and training materials for health professionals, patients and their relatives, and society as a whole. Finally, it supports a rational and fair selection of all those ethical issues that should be addressed in health policies, position papers and clinical practice guidelines. Further research is needed to identify ways to systematically select the most relevant ethical issues not only in the clinical environment, but also for the development of clinical practice guidelines.

Forekomst Europa og Nord-Amerika

Tab. 23: Systematiske oversikter om forekomst av ALS i Europa og Nord-Amerika

	Referanse	Sammendrag
1.	Marin B, Boumediene F, Logroscino G, Babron MC, Leutenegger AL, Preux PM, et al. **Ethnic differences in incidence of amyotrophic lateral sclerosis**. Neuroepidemiology 2014;43 (3-4):167-168.	Background: Amyotrophic Lateral Sclerosis is a rare neurodegenerative disorder with a high personal, societal and economic burden. Whether ALS incidence varies with ethnicity is of major interest. Methods: We performed a systematic review and meta-analysis of data concerning the differences in phenotype and outcome of ALS as regard ethnicity. We aimed to produce synthesized epidemiological indicators. Results: This review displays pooled and weighted estimates of ALS crude and standardized incidence of worldwide populationbased studies. Based on a continental approach, significant differences have been reported between Europe and East Asia (China, Japan), South Asia (Iran) and West Asia (Israel). Conversely, homogeneous rates have been reported in Caucasian populations from Europe, North America and New Zealand. A more refined approach involving genomic data confirmed the positive association between ALS incidence and European ancestry and the negative association between ALS incidence and Asian ancestry or admixed populations. Conclusions: This review sets the scene to sustain a collaborative study involving a wide international consortium in order to perform, with homogeneous methodology, an investigation of the link between ancestry, environment, and ALS incidence.
2.	Jette N, Pringsheim T, Day L, De Robles P, Fiest K, Hamilton M, et al. **The international incidence and prevalence of neurological diseases-do we really know how common neurological conditions are? Challenges**	OBJECTIVE: (1) Perform systematic reviews of the incidence/prevalence of 15 neurological conditions; (2) Examine between-study heterogeneity; (3) Discuss issues arising as a result of the heterogeneity in the conduct of international epidemiological studies in neurology. BACKGROUND: In 2009, the Canadian National Population Study of Neurological Conditions was launched. One of its aims was to examine the epidemiology of 15 conditions [Alzheimer's disease/related dementias, amyotrophic lateral sclerosis (ALS), brain tumours, cerebral palsy (CP), dystonia, epilepsy, Huntington disease, hydrocephalus, multiple sclerosis, muscular dystrophy (MD), Parkinson's disease, spina bifida, spinal cord injury (SCI), Tourette syndrome and traumatic brain injury (TBI)]. DESIGN/METHODS: Systematic reviews with meta-analysis (where appropriate) of population-based studies report-

	in interpreting international epidemiological studies. Neurology 2013;80 (1 MeetingAbstracts).	ing on the incidence and/or prevalence of all conditions were conducted. Data were abstracted and study quality assessed in duplicate. Study heterogeneity was examined descriptively (variation in methods of ascertainment, diagnostic criteria, etc.) and using the I2 statistic. RESULTS:~65,000 abstracts and 4,663 articles were reviewed, with data abstracted on >1280 articles (n=16 for dystonia to >200 for spina bifida). Incidence studies were less frequently performed than prevalence studies except for SCI and TBI (few prevalence studies). Within conditions, methodology (ascertainment methods, age group included) and estimates differed substantially between studies. The I2 was lowest for Duchenne MD prevalence in children (67%), ALS incidence (83.6%) and CP prevalence (89.5%) but >90% for most other conditions studied. Study heterogeneity (meta-regressions) and the challenges this poses to the international comparability of data will be discussed. CONCLUSIONS: Significant inconsistencies exist in methodology between epidemiological studies of neurological conditions, resulting in widely differing estimates, even between countries of similar socioeconomic status. There is a need to establish widely accepted standards for epidemiological research on neurological conditions. This would include recommendations regarding common data elements that should be collected and suggested methods of ascertainment and reporting of results.
3.	Chio A, Logroscino G, Traynor BJ, Collins J, Simeone JC, Goldstein LA, et al. **Global epidemiology of amyotrophic lateral sclerosis: a systematic review of the published literature**. Neuroepidemiology 2013;41(2):118-130.	BACKGROUND: Amyotrophic lateral sclerosis (ALS) is relatively rare, yet the economic and social burden is substantial. Having accurate incidence and prevalence estimates would facilitate efficient allocation of healthcare resources. OBJECTIVE: To provide a comprehensive and critical review of the epidemiological literature on ALS. METHODS: MEDLINE and EMBASE (1995-2011) databases of population-based studies on ALS incidence and prevalence reporting quantitative data were analyzed. Data extracted included study location and time, design and data sources, case ascertainment methods and incidence and/or prevalence rates. Medians and interquartile ranges (IQRs) were calculated, and ALS case estimates were derived using 2010 population estimates. RESULTS: In all, 37 articles met the inclusion criteria. In Europe, the median incidence rate (/100,000 population) was 2.08 (IQR 1.47-2.43), corresponding to an estimated 15,355 (10,852-17,938) cases. Median prevalence (/100,000 population) was 5.40 (IQR 4.06-7.89), or 39,863 (29,971-58,244) prevalent cases. CONCLUSIONS: Disparity in rates among ALS incidence and prevalence studies may be due to differences in study design or true variations in population demographics such as age and geography, including environmental factors and genetic predisposition. Additional large-scale studies that use standardized case ascertainment methods are needed to more accurately assess the true global burden of ALS.Copyright © 2013 S. Karger AG, Basel.
4.	Hoppitt T, Pall H, Calvert M, Gill P, Yao G, Ramsay J, et al. **A systematic review of the incidence and prevalence of**	BACKGROUND: Updated, robust estimates of the incidence and prevalence of rare long-term neurological conditions in the UK are not available. Global estimates may be misrepresentative as disease aetiology may vary by location. OBJECTIVES: To systematically review the incidence and prevalence of long-term neurological conditions in the UK since 1988.

	long-term neurological conditions in the UK. Neuroepidemiology 2011;36(1):19-28.	SEARCH STRATEGY: Medline (January 1988 to January 2009), Embase (January 1988 to January 2009), CINAHL (January 1988 to January 2009) and Cochrane CENTRAL databases. SELECTION CRITERIA: UK population-based incidence/prevalence studies of long-term neurological conditions since 1988. Exclusion criteria included inappropriate diagnoses and incomprehensive case ascertainment. DATA COLLECTION AND ANALYSIS: Articles were included based on the selection criteria. Data were extracted from articles with ranges of incidence and prevalence reported. MAIN RESULTS: Eight studies met the criteria (3 on motor neurone disease; 4 on Huntington's disease; 1 on progressive supranuclear palsy). The incidence of motor neurone disease ranged from 1.06 to 2.4/100,000 person-years. The prevalence ranged from 4.02 to 4.91/100,000. The prevalence of Huntington's disease ranged from 4.0 to 9.94/100,000. The prevalence of progressive supranuclear palsy ranged from 3.1 to 6.5/100,000. CONCLUSIONS: The review updates the incidence/prevalence of long-term neurological conditions. Future epidemiological studies must incorporate comprehensive case ascertainment methods and strict diagnostic criteria.Copyright © 2010 S. Karger AG, Basel.
5.	Byrne S, Walsh C, Lynch C, Bede P, Elamin M, Kenna K, et al. **Rate of familial amyotrophic lateral sclerosis: a systematic review and meta-analysis**. Journal of Neurology, Neurosurgery & Psychiatry 2011;82(6):623-627.	BACKGROUND: The population rate of familial amyotrophic lateral sclerosis (FALS) is frequently reported as 10%. However, a systematic review and meta-analysis of the true population based frequency of FALS has never been performed. METHOD: A Medline literature review identified all original articles reporting a rate of FALS. Studies were grouped according to the type of data presented and examined for sources of case ascertainment. A systematic review and meta-analysis of reported rates of FALS was then conducted to facilitate comparison between studies and calculate a pooled rate of FALS. RESULTS: 38 papers reported a rate of FALS. Thirty-three papers were included in analysis and the rate of FALS for all studies was 4.6% (95% CI 3.9% to 5.5%). Restricting the analysis to prospective population based registry data revealed a rate of 5.1% (95% CI 4.1% to 6.1%). The incidence of FALS was lower in southern Europe. There was no correlation between rate of FALS and reported SOD1 mutation rates. CONCLUSION: The rate of FALS among prospective population based registries is 5.1% (CI 4.1 to 6.1%), and not 10% as is often stated. Further detailed prospective population based studies of familial ALS are required to confirm this rate.
6.	Wolfson C, Kilborn S, Oskoui M, Genge A. **Incidence and prevalence of amyotrophic lateral sclerosis in Canada: a systematic review of the**	BACKGROUND: Amyotrophic lateral sclerosis (ALS) is a fatal progressive neurodegenerative disease of unknown etiology. Although known to be rare, precise information on the frequency of ALS is essential to anticipate future demands on health resources and as baseline information for epidemiological studies. As part of a new ALS epidemiological initiative in Canada, we conducted a systematic review of published incidence and prevalence research in Canada. METHODS: Electronic searches and bibliographic reviews of pertinent publications were conducted.

	literature. Neuroepidemiology 2009;33(2):79-88.	RESULTS: We identified 6 published studies from 4 Canadian provinces conducted between 1974 and 2004; 2 were available only as abstracts. Reported annual incidence rates were similar and study quality was generally good, but there was insufficient detail to adequately assess the methodological quality of 3 of the studies. The most recent studies reported an annual ALS age-adjusted incidence of 2.13 per 100,000 in Nova Scotia (2003-2004) and a crude mean annual incidence of 2.4 per 100,000 in Newfoundland and Labrador (2000-2004). CONCLUSIONS: There are limited data on the frequency of ALS in Canada. We found no studies from 6 of the Canadian provinces or from the territories. Future research is needed to estimate the frequency of occurrence of ALS in Canada.Copyright 2009 S. Karger AG, Basel.

Pågående systematiske oversikter – ulike temaer

Tab. 24. Systematiske oversikter under utarbeidelse

	Referanse	Beskrivelse og lenke til protokoll/register
1.	Ng L, Khan F, Young Carolyn A. **Symptomatic treatments for amyotrophic lateral sclerosis/motor neuron disease**. Cochrane Database of Systematic Reviews 2015 (6):CD011776.	The objectives are as follows: To summarise the evidence from Cochrane systematic reviews of all symptomatic treatments for motor neuron disease (MND). If possible, we will compare the effectiveness of agents with similar rationale for use in MND. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011776/abstract
2.	Abdul Wahid SF, Law Zhe K, Lai Nai M, Ismail Nor A, Azman Ali R. **Cell-based therapies for amyotrophic lat-**	The objectives are as follows: To evaluate the efficacy and safety of cell-based therapy in people with ALS/MND compared with a placebo or no additional treatment http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011742/abstract

	eral sclerosis/motor neuron disease. Cochrane Database of Systematic Reviews 2015 (6):CD011742.	
3.	Young Carolyn A, Gibbons C, Pagnini F, Friede T. **Treatment for fatigue in amyotrophic lateral sclerosis/motor neuron disease (ALS/MND)**. Cochrane Database of Systematic Reviews 2014 (3):CD011005.	The objectives are as follows: To assess the effects of pharmacological and non-pharmacological interventions for fatigue in ALS/MND. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011005/abstract
4.	Maguire C, McDermott C, Hind D, Radunovic A, Shaw Pamela J. **Diaphragm pacing systems for amyotrophic lateral sclerosis / motor neuron disease**. Cochrane Database of Systematic Reviews 2014 (11):CD011222.	The objectives are as follows: The primary objectives were to assess the efficacy and safety of diaphragm pacing for the treatment of people with ALS/MND who develop respiratory insufficiency. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011222/abstract
5.	Bongioanni P, Borasio GD, Oliver D, Tramonti F, Romagnoli A, Kapitza KP. **Methods for informing people with amyotrophic lateral sclerosis/motor neuron disease of their diagnosis**. Cochrane Database	The aim of this review is to examine the effects and effectiveness of different methods for informing people with ALS or MND of their diagnosis on their knowledge and understanding of their disease, its treatment and care. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007593/abstract

	of Systematic Reviews 2009;(1)(CD007593).	
6.	Diana A, Sogos V, Bongioanni P, Miller Robert G, Moore Dan H. **Gamma aminobutyric acid (GABA) modulators for amyotrophic lateral sclerosis/motor neuron disease**. Cochrane Database of Systematic Reviews 2006 (2):CD006049.	The objectives are as follows: The primary objective of the review will be to examine the efficacy of gabapentin and baclofen in delaying the progression of ALS. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006049/abstract
7.	Wright C, Muenchberger H, Whitty J. **Disability housing: a systematic review of key housing features to inform residential design and development for adults with a principal neurological health condition.** PROSPERO 2014:CRD42014010751	http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014010751
8.	Siemens V. **Specialist palliative care services for adults with advanced, incurable illness in hospital, hospice or community settings: protocol for a systematic review.** PROSPERO 2015: CRD42015020674	http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015020674

9.	Plentz R, Stein C, Marcolino M, Hauck M, Schardong J. **Effects of transcutaneous electrical nerve stimulation on modulation of spasticity on motor neuron disease: a systematic review of randomized controlled trials.** PROSPERO 2015:CRD42015020146	http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015020146
10.	Ferreira G. **Respiratory training and neurodegenerative disease: systematic review and meta-analysis.** PROSPERO 2015:CRD42015017066	http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015017066
11.	Fayter D, O'Connor J, Booth A, McDaid C, Rodriguez-Lopez R. **Orthotic management of instability of the knee in neuromuscular disease and central nervous system disorders.** PROSPERO 2014:CRD42014010180	http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014010180
12.	de Wit J, Schröder C, Beelen A, van Groenestijn A, Bakker L, van den Berg L, et al. **Caregiver burden in Amyotrophic Lateral Sclerosis:**	http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015019842

	a systematic review. PROSPERO 2015:CRD42015019842	
13.	Annerieke van Groenestijn EK-vR, Johanna Visser-Meily, Leonard van den Berg, Carin Schröder. **Psychological factors and quality of life in ALS** PROSPERO 2015:CRD42015027303	http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015027303
14.	**Motor Neurone Disease.** NICE.	Anticipated publication date: February 2016. https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0680
15.	Yi Z-M, Liu F, Zhai S-D, Belsh J, Zhan S-Y, Schiffman P. **Pharmacological interventions for improving respiratory function in amyotrophic lateral sclerosis**. Cochrane Database of Systematic Reviews 2012 (8):CD010030.	This is the protocol for a review and there is no abstract. The objectives are as follows:To assess the efficacy and safety of pharmacological interventions for providing symptomatic relief or a disease-modifying effect on respiratory function in people with ALS. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010030/abstract;jsessionid=6EF76413FFF9BA4C722C934B9A896CD0.f04t03
16.	Sathasivam S, Addison-Jones R, Miller R, Moore D, Young CA. **Minocycline for amyotrophic lateral sclerosis or motor neuron disease.** Cochrane Database of Systematic Reviews	This is the protocol for a review and there is no abstract. The objectives are as follows: We will systematically review the evidence from randomised trials for the benefits and harms from minocycline for ALS or MND. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006840/abstract

	2007;(4)(CD006840).		

Pågående primærstudier

Nedenstående tabeller viser pågående primærstudier som er registrert i studieregistre med status «pågående» («ongoing») per november 2015. Studiene er sortert alfabetisk på behandlingstiltak. Følg URL til studieregisteret for å mer informasjon om studiens innhold, resultater, status og dato for planlagt ferdigstillelse.

Se rapportens innholdsoversikt for oversikt over tema og sidetall.

Fysioterapi, trening og ergoterapi

Tab. 25: Pågående studier om effekten av fysioterapi, trening og ergoterapi

	Tittel	Land, by Studienummer	URL til studieregister
1.	Accurate Test of Limb Isometric Strength (ATLIS) in ALS	USA NCT02374606	https://ClinicalTrials.gov/show/NCT02374606
2.	Feasibility of a Consumer Based Accelerometer in Monitoring Outpatient Physical Activity: A Study in Patients With Cancer and Amyotrophic Lateral Sclerosis	USA NCT02457715	https://ClinicalTrials.gov/show/NCT02457715

3.	Trial of Resistance and Endurance Exercise in Amyotrophic Lateral Sclerosis (ALS)	USA NCT01521728	https://ClinicalTrials.gov/show/NCT01521728
4.	Prognostic Value of a Diaphragmatic Endurance Test in Patients With Amyotrophic Lateral Sclerosis	Frankrike NCT02528071	https://ClinicalTrials.gov/show/NCT02528071
5.	Effect of Motor Rehabilitation Treatment on Amyotrophic Lateral Sclerosis (ALS)	Italia NCT02306109	https://ClinicalTrials.gov/show/NCT02306109
6.	Aerobic Exercise Training in Amyotrophic Lateral Sclerosis (ENDURANCE)	Italia NCT01650818	https://ClinicalTrials.gov/show/NCT01650818
7.	Muscle Training of Patients With Amyotrophic Lateral Sclerosis (ALS)	Danmark NCT01504009	https://ClinicalTrials.gov/show/NCT01504009
8.	Aerobic Exercise Therapy and Cognitive Behavioural Therapy in Amyotrophic Lateral Sclerosis: effects on activities and quality of life.	Nederland NTR1616	http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=1616
9.	Inspiratory Training in Amyotrophic Lateral Sclerosis - a phase III, multicentre, double-blind, randomised-controlled trial	Australia ACTRN12608000238370	http://www.anzctr.org.au/ACTRN12608000238370.aspx

Legemidler

Tab. 26: Pågående studier om effekten av ulike legemidler

	Tittel	**Land Studienummer**	**URL til studieregister**
1.	Clinical and electromyographic follow-up of patients taking riluzole and lithium carbonate - A randomized controlled trial	Brasil RBR-2n5mtq	http://www.ensaiosclinicos.gov.br/rg/RBR-2n5mtq/
2.	The Safety of Edaravone for patients with Amyotrophic Lateral Sclerosis: Single centered open label trial	Japan UMIN000016352	https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&recptno=R000018985&type=summary&language=E

3.	Trial to look at the nerve conductance in patients with ALS, with and without Riluzole or Retigabine.	Nederland 2015-001431-20	https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-001431-20/NL
4.	Efficacy and Safety Study of MYOBLOC® Followed by Open-Label Multiple-Treatment With MYOBLOC® in the Treatment of Troublesome Sialorrhea in Adult Subjects	USA NCT01994109	https://ClinicalTrials.gov/show/NCT01994109
5.	A Pilot Study of RNS60 in Amyotrophic Lateral Sclerosis (ALS)	USA NCT02525471	https://ClinicalTrials.gov/show/NCT02525471
6.	Determining the Safety of L-serine in ALS	USA NCT01835782	https://ClinicalTrials.gov/show/NCT01835782
7.	A Trial of Tocilizumab in ALS Subjects (TCZALS-001)	USA NCT02469896	https://ClinicalTrials.gov/show/NCT02469896
8.	Mexiletine for the Treatment of Muscle Cramps in ALS	USA NCT01811355	https://ClinicalTrials.gov/show/NCT01811355
9.	Ventilatory Investigation of Tirasemtiv and Assessment of Longitudinal Indices After Treatment for a Year	USA NCT02496767	https://ClinicalTrials.gov/show/NCT02496767
10.	A follow-on Study to Assess Long-term Safety and Tolerability of i.c.v Administration of sNN0029 in Patients With ALS	Sverige NCT02269436	https://ClinicalTrials.gov/show/NCT02269436
11.	A Pilot Study of Inosine in ALS	USA NCT02288091	https://ClinicalTrials.gov/show/NCT02288091
12.	Therapy in Amyotrophic Lateral Sclerosis With Memantine at 20 mg BID (TAME)	USA NCT02118727	https://ClinicalTrials.gov/show/NCT02118727
13.	A Registry-Based Clinical Trial of Pimozide in Patients With Neuromuscular Junction Transmission Dysfunction Due to ALS	Canada NCT02463825	https://ClinicalTrials.gov/show/NCT02463825
14.	A Safety Study of sNN0029 Administration Via Intracerebroventricular Route to Patients With ALS	Sverige NCT01999803	https://ClinicalTrials.gov/show/NCT01999803

15.	SOD1 Inhibition by Pyrimethamine in Familial Amyotrophic Lateral Sclerosis (ALS)	USA NCT01083667	https://ClinicalTrials.gov/show/NCT01083667
16.	Effects of ODM-109 on Respiratory Function in Patients With Amyotrophic Lateral Sclerosis	Finland NCT02487407	https://ClinicalTrials.gov/show/NCT02487407
17.	Clinical Trial Nuedexta in Subjects With ALS	USA NCT01806857	https://ClinicalTrials.gov/show/NCT01806857
18.	Clinical Trial of Ezogabine (Retigabine) in ALS Subjects	USA NCT02450552	https://ClinicalTrials.gov/show/NCT02450552
19.	Efficacy, Safety and Tolerability of High Lipid and Calorie Supplementation in Amyotrophic Lateral Sclerosis	Tyskland NCT02306590	https://ClinicalTrials.gov/show/NCT02306590
20.	Immuno-modulation in Amyotrophic Lateral Sclerosis- a Phase II Study of Safety and Activity of Low Dose Interleukin-2	Frankrike NCT02059759	https://ClinicalTrials.gov/show/NCT02059759
21.	Rasagiline in Subjects With Amyotrophic Lateral Sclerosis (ALS)	USA NCT01786603	https://ClinicalTrials.gov/show/NCT01786603
22.	Efficacy and Safety of Plasma Exchange With Albumin in Patients With Amyotrophic Lateral Sclerosis	Spania NCT02479802	https://ClinicalTrials.gov/show/NCT02479802
23.	Oral Nutritional Supplementation in Amyotrophic Lateral Sclerosis (ALS) Patients	Frankrike NCT02152449	https://ClinicalTrials.gov/show/NCT02152449
24.	Safety Study of VM202 to Treat Amyotrophic Lateral Sclerosis	USA NCT02039401	https://ClinicalTrials.gov/show/NCT02039401
25.	Ibudilast (MN-166) in Subjects With Amyotrophic Lateral Sclerosis (ALS)	USA NCT02238626	https://ClinicalTrials.gov/show/NCT02238626
26.	HERV-K Suppression Using Antiretroviral Therapy in Volunteers With Amyotrophic Lateral Sclerosis (ALS)	USA NCT02437110	https://ClinicalTrials.gov/show/NCT02437110
27.	Phase II/III Randomized, Placebo-controlled Trial of Arimoclomol in SOD1 Positive Familial Amyotrophic Lateral Sclerosis	USA NCT00706147	https://ClinicalTrials.gov/show/NCT00706147

28.	Stemals-II	Italia 2014-002228-28	https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-002228-28/IT
29.	Safety and Efficacy of Apovir for treatment of patients with ALS (Amyotrophic lateral sclerosis)	Sverige 2012-002099-15	https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-002099-15/SE
30.	Open randomized controlled trial of the Jianpi Yifei Decoction in the treatment of bulbar paralysis of amyotrophic lateral sclerosis	Kina ChiCTR-IOR-14005674	http://www.chictr.org.cn/showproj.aspx?proj=10035
31.	Tamoxifen Treatment in Patients With Motor Neuron Disease	Taiwan NCT02166944	https://ClinicalTrials.gov/show/NCT02166944
32.	sCD163 in ALS Patients	Danmark NCT02325375	https://ClinicalTrials.gov/show/NCT02325375
33.	An Open Label, Safety and Tolerability Continuation Study of Intracerebroventricular Administration of sNN0029 to Patients With Amyotrophic Lateral Sclerosis	Belgia NCT01384162	https://ClinicalTrials.gov/show/NCT01384162
34.	Immunosuppression in Amyotrophic Lateral Sclerosis (ALS)	USA NCT01884571	https://ClinicalTrials.gov/show/NCT01884571
35.	Study of Rasagiline in Patients With Amyotrophic Lateral Sclerosis	Tyskland NCT01879241	https://ClinicalTrials.gov/show/NCT01879241
36.	A Study to Explore the Safety and Tolerability of Acthar in Patients With Amyotrophic Lateral Sclerosis	USA NCT01906658	https://ClinicalTrials.gov/show/NCT01906658
37.	A Long-Term Study in Patients With Amyotrophic Lateral Sclerosis (ALS)	Japan NCT00445172	https://ClinicalTrials.gov/show/NCT00445172
38.	Assessment of the efficacy and the influence on swallowing function of transdermal scopolamine for ALS patients	Japan UMIN000011494	https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&type=summary&recptno=R000013085&language=E
39.	Safety and Efficacy on Spasticity Symptoms of a Cannabis Sativa Extract in Motor Neuron Disease	Italia NCT01776970	https://ClinicalTrials.gov/show/NCT01776970

40.	A Clinical Trial of Safety and Efficacy of Fasudil in Subjects With Amyotrophic Lateral Sclerosis (ALS)	Kina NCT01935518	https://ClinicalTrials.gov/show/NCT01935518
41.	The effect of Granolocyte Colony Stimulating Factor in treatment of Amyotrophic Lateral Sclerosis	Iran IRCT201207238509N2	http://www.irct.ir/searchresult.php?id=8509&number=2
42.	Efficacy, Safety and Tolerability Study of 1 mg Rasagiline in Patients with Amyotrophic Lateral Sclerosis (ALS) Receiving Standard Therapy (Riluzole)	Tyskland 2011-004482-32	https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-004482-32/DE
43.	Evaluation of masitinib in Amyotrophic Lateral Sclerosis (ALS)	Frankrike 2010-024423-24	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2010-024423-24
44.	Treating Amyotrophic Lateral Sclerosis (ALS) With R(+) Pramipexole Dihydrochloride Monohydrate at 60 mg/Day	USA NCT00596115	https://ClinicalTrials.gov/show/NCT00596115
45.	Trial of Safety and Efficacy of Rasagiline in Patients With Amyotrophic Lateral Sclerosis (ALS)	USA NCT01232738	https://ClinicalTrials.gov/show/NCT01232738
46.	Erythropoietin in Amyotrophic Lateral Sclerosis: a study to identify the best dose and the optimal route of administration and evaluate the safety	Italia 2011-001329-26	https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-001329-26/IT
47.	Clinical Study of Dexpramipexole in Amyotrophic Lateral Sclerosis (ALS)	Spania 2010-022818-19	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2010-022818-19
48.	A fase II, randomized, Double-Blind, Placebo-Controlled, Multicentre Study for the Safety and Efficacy on Spasticity Symptoms of a Cannabis Sativa Extract in Motor Neuron Disease Patients - ND	Italia 2010-022808-40	https://www.clinicaltrialsregister.eu/ctr-search/trial/2010-022808-40/IT
49.	Study of the Role of G72 in Amyotrophic Lateral Sclerosis: Biomarker Discovery and Mechanism Investigation	Kina NCT01378026	https://ClinicalTrials.gov/show/NCT01378026
50.	A 12-week, Multicenter, Safety and Dose-ranging Study of 3 Oral Doses of TCH346 in Patients With Amyotrophic Lateral Sclerosis	USA NCT00036413	https://ClinicalTrials.gov/show/NCT00036413
51.	Olanzapine for the Treatment of Appetite Loss in Amyotrophic Lateral Sclerosis (ALS)	Tyskland NCT00876772	https://ClinicalTrials.gov/show/NCT00876772

52.	Safety and Tolerability of Anakinra in Combination With Riluzol in Amyotrophic Lateral Sclerosis	Tyskland NCT01277315	https://ClinicalTrials.gov/show/NCT01277315
53.	Efficacy and Safety of YAM80 in Amyotrophic Lateral Sclerosis (ALS)	Japan NCT00886977	https://ClinicalTrials.gov/show/NCT00886977
54.	Safety and efficacy of erythropoietin in amyotrophic lateral sclerosis: a randomized, placebo-controlled clinical trial - nd	Italia 2009-016066-91	https://www.clinicaltrialsregister.eu/ctr-search/trial/2009-016066-91/IT
55.	Phase II/III, multicenter, randomized, parallel group,double-blind, placebo controlled study to assess safety and efficacy of TRO19622 in Amyotrophic Lateral Sclerosis (ALS) patients treated with riluzole	Frankrike 2008-007320-25	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2008-007320-25
56.	Clinical Trial of Vitamin E to Treat Muscular Cramps in Patients With ALS	Canada NCT00372879	https://ClinicalTrials.gov/show/NCT00372879
57.	A Multi-Center Controlled Screening Trial of Safety and Efficacy of Lithium Carbonate in Subjects With Amyotrophic Lateral Sclerosis (ALS)	USA NCT00790582	https://ClinicalTrials.gov/show/NCT00790582
58.	Cistanche Total Glycosides for Amyotrophic Lateral Sclerosis: A Randomized Control Trial (RCT) Study Assessing Clinical Response	Kina NCT00753571	https://ClinicalTrials.gov/show/NCT00753571
59.	Lithium trial bij ALS	Nederland NTR1432	http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=1432
60.	Etude de l'effet du carbonate de lithium sur une population de patients atteints de SLA en ouvert en comparaison avec une population de référence. LISLA – LISLA	Frankrike 2008-003707-32	https://www.clinicaltrialsregister.eu/ctr-search/trial/2008-003707-32/FR
61.	A Multinational, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Efficacy, Tolerability and Safety of talampanel in Subjects with Amyotrophic Lateral Sclerosis (ALS)	Frankrike, Belgia m.fl. 2008-002062-62	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2008-002062-62
62.	Single-blind, randomized, parallel group, dose-finding trial on lithium for the treatment of	Italia 2008-001094-15	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2008-001094-15

63.	A Phase II multi-centre, extension study to investigate the long term safety of ONO-2506PO in patients diagnosed with Amyotrophic Lateral Sclerosis (ALS).	Tyskland, Belgia m.fl. 2007-004723-37	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2007-004723-37
64.	MEMANTINA (Ebixa X) PARA LA DISCAPACIDAD FUNCIONAL EN LA ESCLEROSIS LATERAL AMIOTRÓFICA	Spania 2007-002117-39	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2007-002117-39
65.	A randomized, double-blind pilot study vs. placebo for the evaluation of efficacy and tolerability of tauroursodeoxycholic	Italia 2007-001592-10	https://www.clinicaltrialsregister.eu/ctr-search/trial/2007-001592-10/IT
66.	Flecainide in amyotrophic lateral sclerosis - a potential neuroprotective strategy.	Australia ACTRN12608000338369	http://www.anzctr.org.au/ACTRN12608000338369.aspx
67.	Untersuchung der Dosis-Wirk-Beziehung unterschiedlicher Erythropoetin-Dosen auf Frataxin bei Friedreich Ataxie	Østerrike 2007-004919-55	https://www.clinicaltrialsregister.eu/ctr-search/trial/2007-004919-55/AT
68.	A comparison of the effect of Atropine and Botulinum-toxin in patients with severe drooling	Sverige 2007-003017-14	https://www.clinicaltrialsregister.eu/ctr-search/trial/2007-003017-14/SE
69.	A multi-centre,randomised,double blind,placebo controlled,parallel group study to investigate efficacy and safety of ono-2506po compared to placebo,in the presence of riluzole,to patients diagnosed with amyotrophic lateral sclerosis(als), who have had onset of muscle weakness within 14 months of randomization	Italia, Belgia m.fl. 2006-002660-26	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2006-002660-26
70.	A multi-national, multi-centre, randomized, double-blind, placebo-controlled, parallel-group study to assess the efficacy, tolerability and safety of 40 mg glatiramer acetate injection in subjects with amyotrophic lateral sclerosis (ALS) - n.a.	Storbritannia m.fl. 2006-001688-49	https://www.clinicaltrialsregister.eu/ctr-search/trial/2006-001688-49/GB
71.	Multicenter, double-blind, randomized, placebo-controlled, trial on alpha-lipoic acid for the treatment of amyotrophic lateral sclerosis alals - alals	Italia 2005-005152-40	https://www.clinicaltrialsregister.eu/ctr-search/trial/2005-005152-40/IT
72.	Wirksamkeit von oralem Vitamin C bei der Seekrankheit	Tyskland 2005-002211-24	https://www.clinicaltrialsregister.eu/ctr-search/trial/2005-002211-24/DE

73.	Open-Label Extension Study to Investigate the Continued Safety and Effect of ONO 2506PO (1200 mg OD).	Spania 2004-002912-27	https://www.clinicaltrialsregister.eu/ctr-search/trial/2004-002912-27/ES
74.	Study of Creatine Monohydrate in Patients With Amyotrophic Lateral Sclerosis	USA NCT00069186	https://ClinicalTrials.gov/show/NCT00069186

Lysbehandling (fototerapi)

Tab. 27: Pågående studier på effekten av lysbehandling

	Tittel	Land Studienummer	URL til studieregister
1.	Narrow band ultraviolet B (UVB) phototherapy in amyotrophic lateral sclerosis	Australia ACTRN12615000802505	http://www.anzctr.org.au/ACTRN12615000802505.aspx

Magnetisk stimulering

Tab. 28: Pågående studier på effekten av magnetisk stimulering

	Tittel	Land Studienummer	URL til studieregister
1.	Brain and Nerve Stimulation for Hand Muscles in Spinal Cord Injury and ALS	USA NCT02469675	https://ClinicalTrials.gov/show/NCT02469675
2.	Transcranial Direct Current Stimulation as a Novel Therapeutic Approach in Amyotrophic Lateral Sclerosis	Italia NCT01569958	https://ClinicalTrials.gov/show/NCT01569958
3.	The effect of repetitive conditioning transcranial magnetic stimulation on motor cortex excitability in neurodegenerative diseases	Japan UMIN000004371	https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&type=summary&recptno=R000005227&language=E

Menneske-maskin interaksjon

Tab. 29: Pågående studier om effekten av ulike former for menneske-maskin interaksjon

	Tittel	Land Studienummer	URL til studieregister
1.	A New Eye-based Communication Device for ALS Patients	Frankri- keNCT02313402	https://ClinicalTrials.gov/show/NCT02313402
2.	An In-home Study of Brain Computer Interfaces	USA NCT01123200	https://ClinicalTrials.gov/show/NCT01123200
3.	EEG-Based Brain-Computer Interface Project for Individuals With Amyotrophic Lateral Sclerosis (ALS)	USA NCT00718458	https://ClinicalTrials.gov/show/NCT00718458
4.	Communication by Brain - Computer Interface in Amyotrophic Lateral Sclerosis:Feasibility Study	Frankrike NCT01897818	https://ClinicalTrials.gov/show/NCT01897818
5.	Clinical research on brain machine interfaces for motor and communication control	Japan UMIN000007676	https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&type=summary&recptno=R000009045&language=E
6.	Developmental research of communication devices based on the brain machine interface using electroencephalograms	Japan UMIN000002276	http://www.umin.ac.jp/ctr/index.htm
7.	BrainGate2: Feasibility Study of an Intracortical Neural Interface System for Persons With Tetraplegia	USA NCT00912041	https://ClinicalTrials.gov/show/NCT00912041

Organisering

Tab. 30: Pågående studier om organisering av behandling

	Tittel	Land, by Studienummer	URL til studieregister
1.	Case management in patients with Amyotrophic Lateral Sclerosis and their caregivers	Nederland NTR1270	http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=1270

Pårørende

Tab. 31: Pågående studier om tiltak rettet mot pårørende

	Tittel	Land Studienummer	URL til studieregister
1.	Dignity Therapy: A Psychotherapeutic Intervention to Enhance the End of Life Experience for Persons with Motor Neurone Disease and their Family Carers	Australia ACTRN12611000410954	http://www.anzctr.org.au/ACTRN12611000410954.aspx
2	Trial of Ascertaining Individual Preferences for Loved One's Role in End-of-Life	USA NCT01160367	https://ClinicalTrials.gov/show/NCT01160367

Ventilasjonsstøtte

Tab. 32: Pågående studier på effekten av ventilasjonsstøtte

	Tittel	Land Studienummer	URL til studieregister
1.	Nocturnal PtcCO2 Monitoring in Patients With Amyotrophic Lateral Sclerosis (ALS)	Frankrike NCT00879593	https://ClinicalTrials.gov/show/NCT00879593
2.	New Perspectives of Adaptation to NIV in ALS	Italia NCT02537132	https://ClinicalTrials.gov/show/NCT02537132
3.	Diaphragm Pacing System (DPS) In Participants With Amyotrophic Lateral Sclerosis (ALS)	USA NCT01938495	https://ClinicalTrials.gov/show/NCT01938495
4.	European Home Mechanical Ventilation Registry	Tyskland NCT02315339	https://ClinicalTrials.gov/show/NCT02315339
5.	Monitoring of Non-invasive Ventilation During Sleep in ALS	Belgia NCT01889043	https://ClinicalTrials.gov/show/NCT01889043
6.	Humanitarian Device Exemption Post-Approval Study of NeuRx Diaphragm Pacing System for Amyotrophic Lateral Sclerosis	USA NCT01605006	https://ClinicalTrials.gov/show/NCT01605006
7.	Non-invasive Ventilation in Amyotrophic Lateral Sclerosis (ALS) Using the iVAPS Mode	Canada NCT01746381	https://ClinicalTrials.gov/show/NCT01746381
8.	Impact of Early Non Invasive Ventilation in Amyotrophic Lateral Sclerosis (ALS) Patients	Spania NCT01641965	https://ClinicalTrials.gov/show/NCT01641965
9.	Effect of Noninvasive Ventilation on Lung Function in Amyotrophic Lateral Sclerosis	USA NCT00537446	https://ClinicalTrials.gov/show/NCT00537446
10.	Polysomnography-directed Noninvasive Ventilation in Amyotrophic Lateral Sclerosis (ALS)	USA NCT01363882	https://ClinicalTrials.gov/show/NCT01363882
11.	Non-Invasive Ventilation in Amyotrophic Lateral Sclerosis	Italia NCT00560287	https://ClinicalTrials.gov/show/NCT00560287

12.	Optimizing NIPPV Use for Patients With ALS	USA NCT01035476	http://clinicaltrials.gov/show/NCT01035476
13.	Motor-Point Stimulation for Conditioning the Diaphragm of Patients With Amyotrophic Lateral Sclerosis (ALS)	USA NCT00420719	https://ClinicalTrials.gov/show/NCT00420719
14.	Early Treatment of Amyotrophic Lateral Sclerosis (ALS) With Nutrition and Non-Invasive Positive Pressure Ventilation (NIPPV)	USA NCT00116558	https://ClinicalTrials.gov/show/NCT00116558

Stamcellebehandling / genterapi

Tab. 33: Pågående studier om effekten av stamcellebehandling eller genterapi

	Tittel	**Land** **Studienummer**	**URL til studieregister**
1.	Intravenous Injection of Adipose Derived Mesenchymal Stem Cell for ALS	Iran NCT02492516	https://ClinicalTrials.gov/show/NCT02492516
2.	Development of iPS From Donated Somatic Cells of Patients With Neurological Diseases	Israel NCT00874783	https://ClinicalTrials.gov/show/NCT00874783
3.	Derivation of Induced Pluripotent Stem Cells From an Existing Collection of Human Somatic Cells	Israel NCT00801333	https://ClinicalTrials.gov/show/NCT00801333
4.	Phase 2, Randomized, Double Blind, Placebo Controlled Multicenter Study of Autologous MSC-NTF Cells in Patients With ALS	USA NCT02017912	https://ClinicalTrials.gov/show/NCT02017912
5.	Clinical Trial Phase I/II, Randomized, Controlled With Placebo, Triple Blind to Evaluate Safety, and Indications of Efficiency of the Intravenous Administration of the Therapy With 3 Doses of MSC in Patients With ASL Moderated to Severe	Spania NCT02290886	https://ClinicalTrials.gov/show/NCT02290886
6.	Human Neural Stem Cell Transplantation in Amyotrophic Lateral Sclerosis (ALS)	Italia NCT01640067	https://ClinicalTrials.gov/show/NCT01640067

7.	A Dose-escalation Safety Trial for Intrathecal Autologous Mesenchymal Stem Cell Therapy in Amyotrophic Lateral Sclerosis	USA NCT01609283	https://ClinicalTrials.gov/show/NCT01609283
8.	Study to Investigate the Safety of the Transplantation (by Injection) of Human Glial Restricted Progenitor Cells (hGRPs; Q-Cells®) Into Subjects With Amyotrophic Lateral Sclerosis (ALS)	USA NCT02478450	https://ClinicalTrials.gov/show/NCT02478450
9.	Dose Escalation and Safety Study of Human Spinal Cord Derived Neural Stem Cell Transplantation for the Treatment of Amyotrophic Lateral Sclerosis	USA NCT01730716	https://ClinicalTrials.gov/show/NCT01730716
10.	Safety Study of VM202 to Treat Amyotrophic Lateral Sclerosis	USA NCT02039401	https://ClinicalTrials.gov/show/NCT02039401
11.	An Exploratory Clinical Trial to Assess Treatment of Amyotrophic Lateral Sclerosis With Brain Transplants of Autologous Adipose-Tissue Derived Stem Cells (ADSCs)	Kina NCT02383654	https://ClinicalTrials.gov/show/NCT02383654
12.	Clinical Trial on The Use of Autologous Bone Marrow Stem Cells in Amyotrophic Lateral Sclerosis (Extension CMN/ELA)	Spania NCT01254539	https://ClinicalTrials.gov/show/NCT01254539
13.	Pilot study to evaluate the effect of plasma exchange with albumin in patients with amyotrophic lateral sclerosis	Spania 2013-004842-40	https://www.clinicaltrialsregister.eu/ctr-search/trial/2013-004842-40/ES
14.	Combination Therapy of Cord Blood and G-CSF for Patients With Brain Injury or Neurodegenerative Disorders	Korea NCT02236065	https://ClinicalTrials.gov/show/NCT02236065
15.	Mesenchymal Stem Cell Injection in Amyotrophic Lateral Sclerosis	Iran NCT02116634	https://ClinicalTrials.gov/show/NCT02116634
16.	Intramuscular Infusion of Autologous Bone Marrow Stem Cells in Patients With Amyotrophic Lateral Sclerosis	Spania NCT02286011	https://ClinicalTrials.gov/show/NCT02286011
17.	Safety/Efficacy Study for the Biological Treatment of Amyotrophic Lateral Sclerosis With Autologous Stem/Progenitor Cells	Polen NCT02193893	https://ClinicalTrials.gov/show/NCT02193893
18.	Human Spinal Cord Derived Neural Stem Cell Transplantation for the Treatment of Amyotrophic Lateral Sclerosis	USA NCT01348451	https://ClinicalTrials.gov/show/NCT01348451

19.	Autologous Cultured Mesenchymal Bone Marrow Stromal Cells Secreting Neurotrophic Factors (MSC-NTF), in Patients With Amyotrophic Lateral Sclerosis (ALS)	Israel NCT01777646	https://ClinicalTrials.gov/show/NCT01777646
20.	Cell Therapy for Motor Neuron Disease/Amyotrophic Lateral Sclerosis	India NCT02242071	https://ClinicalTrials.gov/show/NCT02242071
21.	Development of human cellular models for motor neuron diseases using disease-specific induced pluripotent stem (iPS) cells	Japan UMIN000011542	https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&type=summary&recptno=R000013490&language=E
22.	A phase I/II clinical trial of the bone marrow's autologous stem cells in patients with amyotrophic lateral sclerosis	Spania 2011-004801-25	https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-004801-25/ES
23.	Safety Study of HLA-haplo Matched Allogenic Bone Marrow Derived Stem Cell Treatment in Amyotrophic Lateral Sclerosis	Korea NCT01758510	https://ClinicalTrials.gov/show/NCT01758510
24.	Clinical trial to value the safety and efficacy of administration of stem cells derived from own patient for the treatment of Amyotrophic Lateral Sclerosis (ALS).	Spania 2011-006254-85	https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-006254-85/ES
25.	The Clinical Trial on the Use of Umbilical Cord Mesenchymal Stem Cells in Amyotrophic Lateral Sclerosis	Kina NCT01494480	https://ClinicalTrials.gov/show/NCT01494480
26.	Efficacy and safety of intraspinal injection of neural stem cell on progression of amyotrophic lateral sclerosis (ALS)	Iran IRCT201107221696N3	http://www.irct.ir/searchresult.php?keyword=&id=1696&number=3&prt=2228&total=10&m=1
27.	Safety and Efficacy of Stem Cell Therapy of Motor Neuron Disease.	Tsjekkia 2011-000362-35	https://www.clinicaltrialsregister.eu/ctr-search/trial/2011-000362-35/CZ
28.	Pilot study on safety and tolerability of repeated mobilization procedures of osteo-medullary derived cells in patients with amyotrophic lateral sclerosis	Italia 2005-003248-75	https://www.clinicaltrialsregister.eu/ctr-search/trial/2005-003248-75/IT

Strålebehandling

Tab. 34: Pågående studie om effekten af strålebehandling

	Tittel		URL til studieregister
1.	Far Infrared Irradiation for Control, Management and Treatment of Amyotrophic Lateral Sclerosis (ALS)	Canada NCT00673140	https://ClinicalTrials.gov/show/NCT00673140

Referanser

1. ALS – muskelsvinnsykdom. Helsenorge.no. [Oppdatert 1. juli 2013; Lest 5. okt. 2015]. Tilgjengelig fra: https://helsenorge.no/sykdom/hjerne-og-nerver/als

2. Amyotrofisk lateral sklerose (ALS) pasientinformasjon. NEL [Oppdatert 3. okt. 2010; Lest 5. okt. 2015]. Tilgjengelig fra: http://nevro.legehandboka.no/sykdommer-og-symptomer/als-pasientinformasjon-33790.html

3. Primærstudier. SFI Campbell. [Lest 23. nov. 2015]. Tilgjengelig fra: http://www.sfi.dk/prim%C3%A6r-studier-252.aspx

4. ClinicalTrials.gov Background. [Lest 23. nov. 2015]. Tilgjengelig fra: https://clinicaltrials.gov/ct2/about-site/background

5. Ordliste 2010. Nasjonalt kunnskapssenter for helsetjenesten. [Lest 23. nov. 2015]. Tilgjengelig fra: http://www.kunnskapssenteret.no/verktoy/ordliste

6. Galvez-Jimenez N. Symptom-based management of amyotrophic lateral sclerosis. UptoDate. [Oppdatert 1. okt. 2015; Lest 23. nov. 2015]. Tilgjengelig fra: http://www.uptodate.com/contents/symptom-based-management-of-amyotrophic-lateral-sclerosis?source=search_result&search=als&selectedTitle=4~64#H13

7. Choudry R, Galvez-Jimenez N, Cudkowicz ME. Disease modifying treatment of amyotrophic lateral sclerosis. UptoDate. [Oppdatert 18. mar. 2015; Lest 23. nov. 2015]. Tilgjengelig fra: http://www.uptodate.com/contents/disease-modifying-treatment-of-amyotrophic-lateral-sclerosis?source=search_result&search=als&selectedTitle=6~64

Vedlegg

Vedlegg 1: Søkestrategi

Søk 1: Systematiske oversikter
Dato for siste søk: 23.11.2015

Databaser søkt: MEDLINE, Embase, PsycINFO, CINAHL, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessments Database (HTA), Epistemonikos, PubMed, Prospero.
Søketreff totalt: 2205
Søketreff etter dublettkontroll: 1750

Epistemonikos
Overviews: 1
Systematic reviews: 72
Structured summaries: 17

(title:(als OR "amyotrophic lateral scleroses" OR "amyotrophic lateral sclerosis" OR "charcot disease" OR (gehrig* AND disease) OR "guam disease" OR "motor neuron disease" OR "motoneuron disease") OR abstract:(als OR "amyotrophic lateral scleroses" OR "amyotrophic lateral sclerosis" OR "charcot disease" OR (gehrig* AND disease) OR "guam disease" OR "motor neuron disease" OR "motoneuron disease"))

Ovid MEDLINE, Embase, PsycINFO

Søketreff totalt: 2221
Embase 1980 to 2015 Week 26: 1047
MEDLINE In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to Present: 737
PsycINFO 1806 to June Week 4 2015: 437

Søketreff totalt etter Ovid dublettkontroll: 1415
Embase 1980 to 2015 Week 26: 999
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to Present: 145
PsycINFO 1806 to June Week 4 2015: 271

1. (amyotrophic* lateral scleros* or ALS or (charcot* adj4 (disease or disorder)) or lou gehrig* or (gehrig* adj (disease* or syndrom*)) or (guam* adj (disease* or syndrom*)) or moto* neuron* disease* or moto?neuron* disease*).tw.
2. Amyotrophic Lateral Sclerosis/
3. Motor Neuron Disease/ or Charcot-Marie-Tooth Disease/
4. 1 or 2 or 3
5. (((systematic* or literature or evidence*) adj2 (review* or overview*)) or meta-anal* or (search* adj3 (literature or database* or systematic*)) or (review* and (medline or pubmed))).mp,pt.
6. (meta-synthes* or meta-ethnograph* or research synthes* or meta-study or narrative synthes* or meta narrative synthes* or critical interpretive synthes*).mp.
7. integrative review*.mp.
8. 5 or 6 or 7
9. 4 and 8
10. 9 use pmoz [MEDLINE]
11. *amyotrophic lateral sclerosis/ or *motor neuron disease/ or *hereditary motor sensory neuropathy/
12. (1 or 11) and 8
13. 12 use emez [Embase]
14. amyotrophic lateral sclerosis/ or Charcot-Marie-Tooth Disease/
15. 1 or 14
16. (meta analysis or "systematic review").md.
17. 8 or 16
18. 15 and 17
19. 18 use psyh [PsycINFO]
20. 10 or 13 or 19
21. remove duplicates from 20

Cinahl

Søketreff: 174

S11 S4 AND S10
S10 S5 OR S6 OR S7 OR S8 OR S9
S9 TI integrative review* OR AB integrative review*
S8 TI ((meta-synthes* or meta-ethnograph* or research synthes* or meta-study or narrative synthes* or critical interpretive synthes*)) OR AB ((meta-synthes* or meta-ethnograph* or research synthes* or meta-study or narrative synthes* or critical interpretive synthes*))
S7 TI ((((systematic* or literature or evidence*) N2 (review* or overview*)) or meta-anal* or (search* N3 (literature or database* or systematic*)) or (review* and (medline or pubmed)))) OR AB ((((systematic* or literature or evidence*) N2 (review* or overview*)) or meta-anal* or (search* N3 (literature or database* or systematic*)) or (review* and (medline or pubmed))))
S6 (MH "Meta Analysis")
S5 (MH "Systematic Review")
S4 S1 OR S2 OR S3
S3 TI ((amyotrophic* lateral scleros* or ALS or (charcot* and (disease or disorder)) or lou gehrig* or (gehrig* N0 (disease* or syndrom*)) or (guam* N0 (disease* or syndrom*)) or moto* neuron* disease* or moto?neuron* disease*)) OR AB ((amyotrophic* lateral scleros* or ALS or (charcot* and (disease or disorder)) or lou gehrig* or (gehrig* N0 (disease* or syndrom*)) or (guam* N0 (disease* or syndrom*)) or moto* neuron* disease* or moto?neuron* disease*))
S2 (MH "Motor Neuron Diseases")
S1 (MH "Amyotrophic Lateral Sclerosis")

Cochrane Library

Linje 1-5: Cochrane Database of Systematic Reviews (tekstord avgrenset til tittel og sammendrag)
Linje 6-7: DARE og HTA (søkt i «all text»)

Søketreff:
Cochrane Database of Systematic Reviews 259
DARE: 40
HTA: 26

#1 MeSH descriptor: [Amyotrophic Lateral Sclerosis] explode all trees
#2 MeSH descriptor: [Motor Neuron Disease] this term only
#3 MeSH descriptor: [Charcot-Marie-Tooth Disease] explode all trees
#4 ((amyotrophic* next lateral next scleros*) or ALS or (chargot* near/4 (disease or disorder)) or (lou next gehrig*) or (gehrig* next (disease* or syndrom*)) or (guam* next (disease* or syndrom*)) or (moto* next neuron* next disease*) or (moto?neuron* next disease*)):ti,ab,kw
#5 #1 or #2 or #3 or #4
#6 ((amyotrophic* next lateral next scleros*) or ALS or (chargot* near/4 (disease or disorder)) or (lou next gehrig*) or (gehrig* next (disease* or syndrom*)) or (guam* next (disease* or syndrom*)) or (moto* next neuron* next disease*) or (moto?neuron* next disease*))
#7 #1 or #2 or #3 or #6
#8 neurodegenerative:ti
#9 #7 or #8

CRD Databases (DARE og HTA)
Søketreff DARE: 40
HTA: 17

1 MeSH DESCRIPTOR Amyotrophic Lateral Sclerosis EXPLODE ALL TREES
2 MeSH DESCRIPTOR Charcot-Marie-Tooth Disease EXPLODE ALL TREES
3 MeSH DESCRIPTOR Motor Neuron Disease EXPLODE ALL TREES
4 (als or Amyotrophic Lateral Sclerosis):TI
5 #1 OR #2 OR #3 OR #4
6 (#1 OR #2 OR #3 OR #4) IN DARE, HTA

PubMed
Søketreff: 88
(amyotrophic lateral sclerosis or ALS or lou gehrig or guam disease or motor neuron disease) and (systematic review or integrative review or meta-analysis or meta-analys* or meta ethnography) AND publisher [sb]

Prospero
Søketreff: 14

Amyotrophic lateral sclerosis (all fields) or als (all fields) or motor neuron disease (all fields) or gehrig* (all fields)

SBU, FINOHTA, CADTH, Sundhedsstyrelsen
Søketreff: 5
Fritekstsøk «amyotrofisk»

PEDRO
Advanced search 1: amyotrophic lateral sclerosis
23

Advanced search 2: motor neuron disease*
10

OT Seeker
Søketreff: 4

Advanced **s**earch
Title/abstract: amyotrophic lateral sclerosis
Sorted by method: systematic reviews

<u>Søk 2 Pågående studier</u>

Clinical Trials.gov
Search by topic - conditions: Amyotrophic lateral sclerosis: 286 studies
Search by topic - conditions: Motor neuron disease: 282 studies

WHO International Clinial Trials Registry Platform
Advanced search – condition: amyotrophic lateral sclerosis
Recruitment status: ALL
Søketreff: 371

www.fhi.no

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