

# Fremtidige konsensusprogrammer ?

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Amyotrofisk Lateral  
Sklerose?

Andre?

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# Dansk ALS-Referenceprogram

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Udarbejdet af gruppe under ALS-selskab,  
udgivet af Dansk Neurologisk Selskab 1998:

Lene Werdelin, Hans Henrik Hinge, Peter  
Brøgger Christensen, Ole Gredal, Palle  
Strange, Birger Johnsen m.fl.



# Indholdsfortegnelse: 1/4

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1. Forord
2. Problemområde
3. Resultat- og procesmål for referenceprogrammet
4. Nuværende viden om Amyotrofisk Lateral Sklerose
  - 4.1. Sygdommen ALS
  - 4.2. Symptomer, kliniske fund og ALS-diagnosen
  - 4.3. Epidemiologi
  - 4.4. Prognose
  - 4.5. Ætiologi og patogenese
  - 4.6. Behandling



# Indholdsfortegnelse: 2/4

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## 5. Organisation og hele patientforløb

5.1. ALS-behandlerteam

5.2. ALS-patientens hospitalsforløb

5.3. Ambulant efterforløb

5.4. Forløb i hjemkommunen

5.5. Det terminale forløb

5.6. Kontaktbog

## 6. ALS-udredningsprogram

# Indholdsfortegnelse: 3/4

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## 7. Understøttende behandling

- 7.1. Kraftnedsættelse og muskelatrofi
- 7.2. Bulbære symptomer
- 7.3. Spasticitet, spasmer og muskelkramper
- 7.4. Smerter
- 7.5. Emotionel inkontinens
- 7.6. Angst og depression
- 7.7. Respirationsproblemer
- 7.8. Terminalfasen

## 8. Patient- og pårørendegrupper

## 9. Sundhedsøkonomiske overvejelser

## 10. Kvalitetssikring og implementering

# Indholdsfortegnelse: 4/4

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## 10. Kvalitetssikring og implementering

10.1. Centralisering af ALS-behandlingen

10.2. Implementering og økonomiske forudsætninger

10.3. Kvalitetssikring

10.4. Revision af referenceprogrammet, ALS-database

## 11. Tillæg til referenceprogrammet

Appendix A: Neurofysiologiske undersøgelser ved ALS

Appendix B: Vejledende retningslinier for behandling med Rilutek®

# Europæiske guidelines

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Good practice in the management of amyotrophic lateral sclerosis: Clinical guidelines. An evidence-based review with good practice points. EALSC Working Group

Andersen PM, Eur J Neurol, 12:921-38, 2005

Andersen PM, Amyotrophic Lateral Sclerosis. 8:195-213, 2007

# Members of the Task Force on Management of Amyotrophic Lateral Sclerosis:

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**Peter M. Andersen, Sverige**

Gian D. Borasio, Tyskland/Italien

Rreinhard Dengler, Tyskland

Orla Hardiman, Irland

Katja Kollwe, Tyskland

Peter Nigel Leigh, England

Pierre-Francois Pradat, Frankrig

Vincenzo Silani, Italien

Barbara Tomik, Polen

# How did they do it?

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- Search strategy: Two investigators screened potentially relevant citations independently.
- We searched the **Cochrane** Central Register of Controlled Trials (CENTRAL) (The Cochrane Library to date); MEDLINE-OVID (January 1966 to date); MEDLINE-ProQuest; MEDLINE-EIFL; EMBASE-OVID (January 1990 to date); Science Citation Index (ISI); The National Research Register; Oxford Centre for Evidenced-based Medicine; American Speech Language Hearing Association (ASHA); the world Federation of Neurology ALS Page of reviews of published research; the Oxford Textbook of Palliative Medicine, and the UK Department of Health National Research Register (<http://www.update-software.com/National/nrr-frame.html>).
- We also searched national neurological databases (like [www.alsa.org](http://www.alsa.org), [alsod.org](http://alsod.org)) and personal collections of references and reference lists of articles.

# Europæiske guidelines

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1. Hurtig udredning og tidlig diagnose
2. Formidling af diagnose
3. Genetisk test og vejledning
4. Medikamentel behandling
5. Multidisciplinært behandlerteam
6. Symptomatisk behandling
7. Kommunikation
8. Ernæring
9. Respiration
10. Palliativ behandling

# Europæiske guidelines

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Opdateres 2009 og udkommer 2010

Emner der mangler?

- Personlighedsændring og Frontotemporal demens
- Topkateder i urinblæren

# Udarbejdelse af nordisk referenceprogram for ALS?

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Er de europæiske guidelines tilstrækkelige?

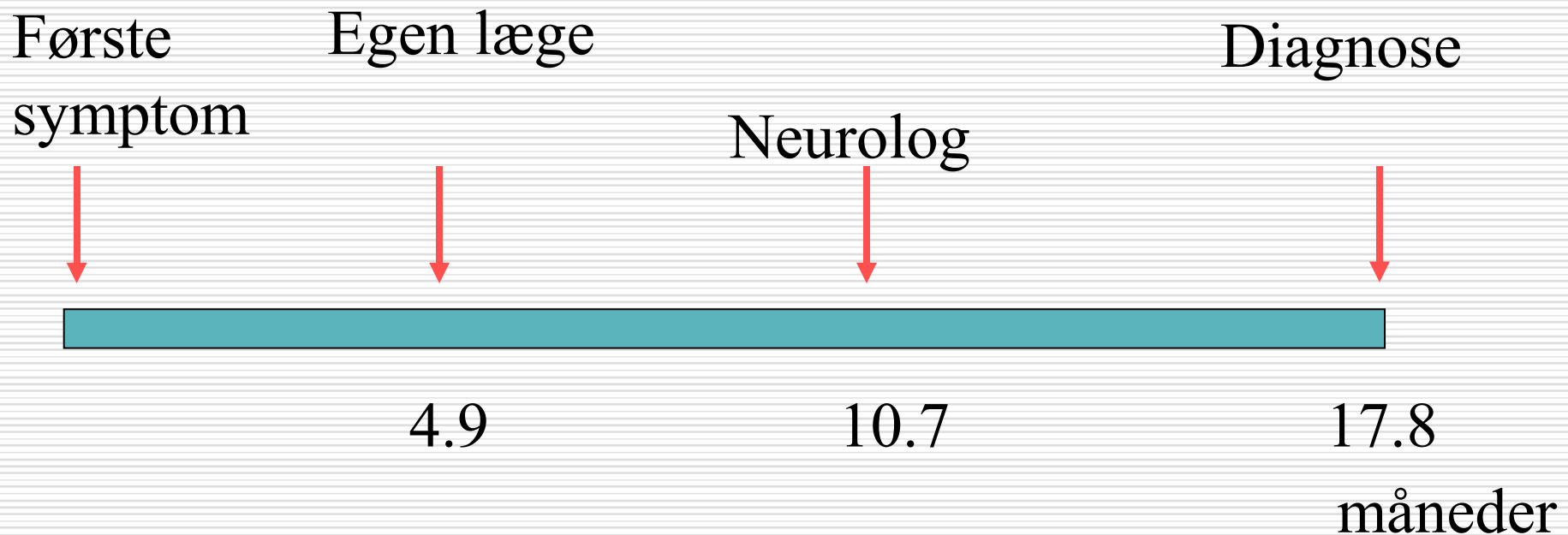
Skal de oversættes til skandinavisk?

Eller skal vi udarbejde vores egne?

# 1. Hurtig udredning og tidlig diagnose?

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91 patienter i Europa Tyskland, Italien, Spanien



Dengler R, Neurology, 1999

# Dansk ALS-database

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ALS-DATABASE

Dansk Selskab for Forskning i  
Amyotrofisk Lateral Sklerose

Databaseansvarlig  
Ole Gredal



# Om ALS: Diagnos:

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Det finns inget specifikt "ALS-prøve".

Diagnosen är en **exklusionsdiagnos**:

*Uteslut övriga sjukdomar med liknande symtombild!*

- 1. Anamnes: Initial asymmetrisk lokaliserad pares med muskelatrofi, ev fascikulationer (kan saknas). Tilltagande symtom.*
- 2. EMG (ökad spontanaktivitet, stora enheter, polyfasi m fl)*
- 3. Neurografi (väsentligen normal)*
- 4. Blodprov analys*
- 5. Ryggmärgsvätska analys*
- 6. DNA analys vid familjär disposition för ALS*

*Feldiagnostik ej ovanligt (5-8% i irländsk resp amerikansk studie).*



Table 1.1

## **Diagnostic criteria for ALS**

The diagnosis of ALS requires the presence of: (positive criteria)

LMN signs (including EMG features in clinically unaffected muscles)

UMN signs

Progression of symptoms and signs

The diagnosis of ALS requires the absence of: (diagnosis by exclusion)

Sensory signs

Sphincter disturbances

Visual disturbances

Autonomic features

Basalganglia dysfunction

Alzheimer-type dementia

ALS "mimic" syndromes (Table 3)

The diagnosis of ALS is supported by:

Fasciculations in one or more regions

Neurogenic changes in EMG

Normal motor and sensory nerve conduction

Absence of conduction block



## 2. Formidling af ALS-diagnosen

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- 85% tilbud om deltagelse af pårørende
- 90% tilbud om opfølgende samtale
- 31% oplyste ikke diagnosen til pt.
- 41% brugte mindre end 30 minutter

Borasio GD, 2001

## 2 Breaking the News: Communicating the Diagnosis

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1. The diagnosis should be communicated by a consultant.
2. The physician should start the consultation by asking what the patient already knows or suspects.
3. Respect the cultural and social background of the patient by asking whether the patient wishes to receive information or prefers that the information be communicated to a family member.
4. The physician should give the diagnosis to the patient and discuss its implications in a **stepwise fashion**, checking repeatedly if the patient understands what is said, and reacting appropriately to the verbal and non-verbal cues of the patient.
5. **The diagnosis should always be given in person and never by mail or telephone, with enough time available (at least 45-60 minutes) on the part of the physician.**
6. Assure the patient that he or her and their family will not be on their own ('abandoned') but will be supported by a professional ALS-care team and with regular follow-up visits to a neurologist. Make arrangements for a **follow-up visit** before the end of the consultation, **ideally within two-four weeks** (or sooner if appropriate).
7. Provide printed materials about the disease and about support and advocacy organizations, about informative websites on the internet.

# 3: ALS og genetik

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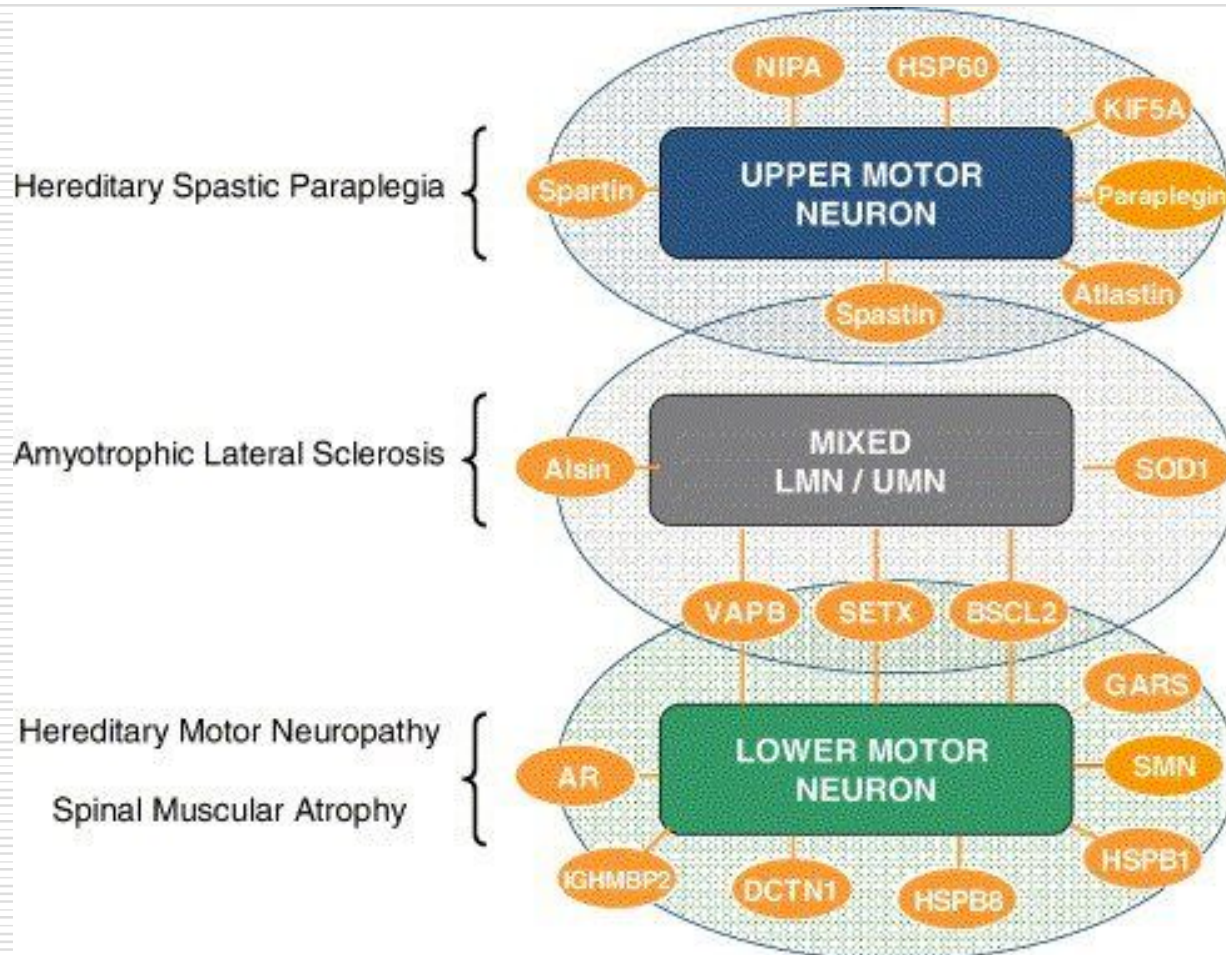
90-95 % sporadiske

5-10 % arvelige (autosomal dominant)

- Superoxid Dismutase 1 (SOD-1): 20%
- Alsin
- Angiogenin
- Dynactin
- Senataxin
- Vesicle ass. Protein B

Orrell 2007, N Engl J Med

# Genetik ved motoriske sygdomme



# 3: Genetic testing and counselling

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- Clinical DNA analysis for SOD1 gene mutation should only be performed in cases with a known familial history of ALS or in SALS cases with the characteristic phenotype of the D90A mutation.
- Clinical DNA analysis for SOD1 gene mutations should *not* be performed in cases with SALS with a typical classical ALS-phenotype.
- Before blood is drawn for DNA analysis, the patient should receive genetic counselling. Give the patient time for consideration. DNA analysis should not be performed without the patients consent.
- Presymptomatic genetic testing should *only* be performed in first degree adult blood-relatives of patients with a known SOD1 gene mutation. Testing should only be performed on a strictly volunteer basis as outlined (*table 6.9*).



# Table 6.9: Guidelines for presymptomatic genetic testing in ALS

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- 1. The test subject should belong to a family with a known SOD1 gene mutation.
- 2. The test subject should be a 1st degree relative of an affected blood relative, or 2nd degree of an affected case if the 1st degree relative is deceased from other causes.
- 3. The test subject should be 18 years or older.
- 4. The test subject should be mentally and physically healthy.
- 5. The test subject should not be under emotional stress (e.g. recently married or divorced, have become unemployed, pregnant etc.).
- 6. The test subject should participate as a volunteer without influence from a third party.
- 7. The test subject should receive a minimum of two genetic counselling sessions before the blood is drawn.
- 8. The test subject can request more than two genetic counselling sessions.
- 9. Genetic counselling should be given by professionals with a specific knowledge about ALS and genetics.
- 10. After the blood sample has been drawn, the mutation analysis should be performed as fast as possible to minimize the emotional discomfort of the procedure.
- 11. The test subject should be informed of the test result at a personal meeting with a genetic counsellor. The test result should never be given by letter or electronic communication.
- 12. It is advisable that the test subject be accompanied by a close friend at the genetic counselling sessions and when the test result is announced.
- 13. The test subject can at any time demand that the blood sample and test records be destroyed.
- 14. The test subject can at any time and without explanation withdraw from the test procedure and choose not to be informed of the test result.
- 15. Professional and community resources should be available to deal with the impact of test result in the test subject and relatives.
- 16. The test result is private and should be kept in a separate file in the medical chart.
- **17. The test result is private and no third party can request taking part in the result.**

# 4. Medikamentel behandling

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Rilutek behandling til ALS anbefales så tidlig som muligt, også til PMA

2-3 mdr. længere overlevelse

Miller, Cochrane Database Syst Rev, 2007

- 4 studier

- 974 rilutek og 503 placebo

# Rilutek overlevelseskurve



WILCOXON  $p = 0.016$

LOGRANK  $p = 0.043$

HOMOGENEITY  $p = 0.708$



# 4. Medikamentel behandling

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Rilutek behandling til ALS:

Ukontrollerede studier med historiske kontroller:

Overlevelse:

6, 10, 12, 14 og 21 måneder

Meininger 2000 , Mitchell 2006, Traynor 2001, Brooks 2001, Turner 2001



# 5. Multidisciplinært behandlerteam

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## ALS-organisation:

14 ALS-team på  
Neurologisk afd.

Respirationscentret  
Øst og Vest

**Patienten  
pårørende**

Egen læge/  
hjemmesygeplejerske

Hospice

Region/kommune

Muskelsvindfonden

Rehabiliteringscenter for muskelsvind

# 5. Multidisciplinært behandlerteam

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## ALS-team funktion

- Udredning - ambulant eller under indlæggelse
- Ambulante besøg i senge- el. dagafsnit hver 2-3 mdr.
- Åben døgnkontakt / åben indlæggelse
- Telefonisk rådgivning
  
- Indlæggelse PEG-sonde og terminaltilstand
- Informere relevante samarbejdspartnere

# 5. Multidisciplinært behandlerteam

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ALS-team på neurologiske afd.

- Neurolog
- Sygeplejerske
- Fysioterapeut
- Ergoterapeut
- Diætist
- Socialrådgiver
- Logopæd
- Psykolog

# Formål med amb.-kontrol

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- Sikring af diagnose
- Monitorering af tilstand mhp. Information, intervention og/eller palliation
  - Fys.
  - Hjælpemidler incl. kommunikationsudstyr
  - Ernæring
  - Sociale forhold incl. hjælpeordning
  - Psykologisk bistand
  - **PEG-sonde**
  - **Respirationshjælp (CPAP, BiPAP, respirator)**

# Indlæggelsesårsager

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- Udredning + diagnose
- Anlæggelse af PEG-sonde
- Vejrtrækningsproblemer
- Andet (angst, eksistentiel krise, aflastning?)
- Terminalforløb

# Informere samarbejdspartnere

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- ALS-team incl. kommunikationscenter
- Praktiserende læge
- Hjemmeplejen
- Kommunal sagsbehandler
- Praktiserende terapeuter
- Rehabil.Center for Muskelsvind
- Resp.Center Øst/Vest

Informere relevante samarbejdspartnere i at være forberedt på sygdommens næste manifestationer

## 6. Symptomatisk behandling

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- Spyttflåd og ufrivillig gaben
- Sekret fra øvre luftveje
- Grådlabilitet
- Kramper/spasmer
- Spasticitet
- Depression, angst og søvnforstyr.
- Smerter
- DVT-forebyggelse

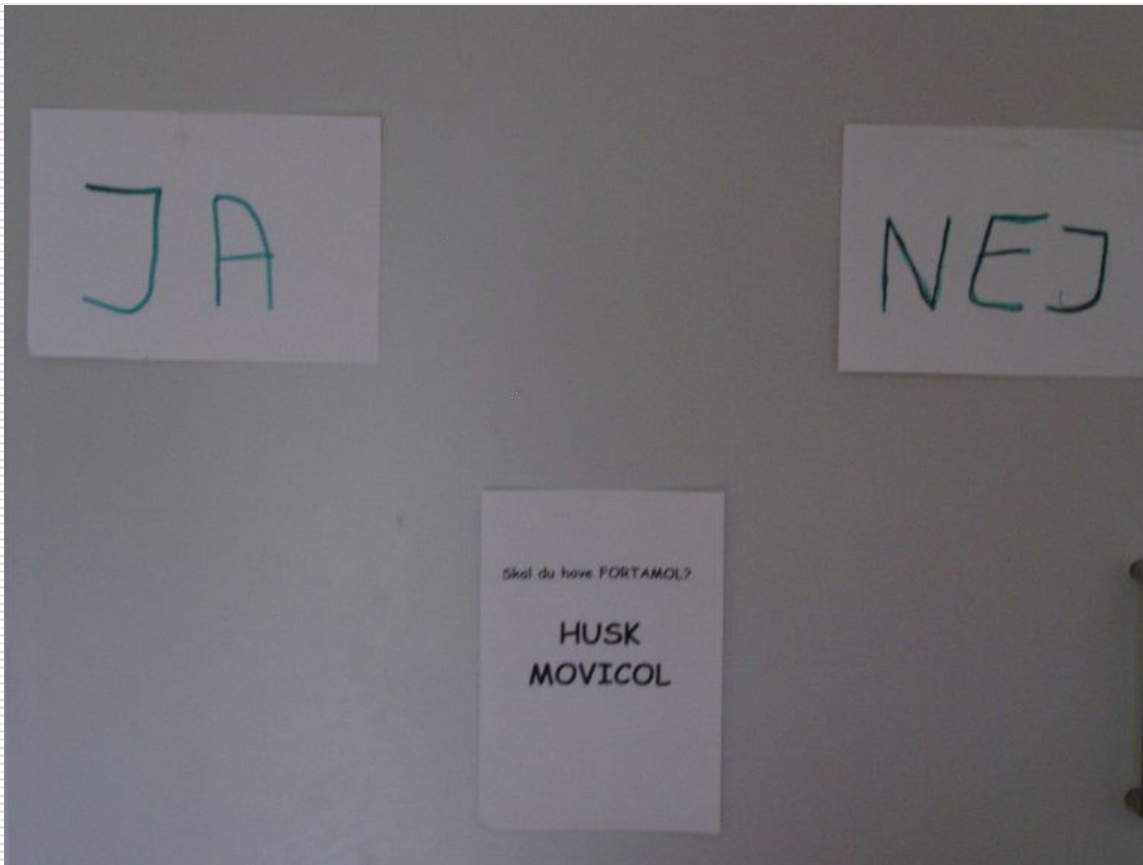
# 7. Kommunikation

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Mulighed for kommunikation er en forudsætning for at bevare patientens fulde integritet og selvbestemmelse.

# 7. Kommunikation

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Sedler på væg fra 39 årig mand med ALS i 2004. De sidste 2½ år tilbragte han på plejehjem og de sidste 6 måneder liggende i sengen.

# 7. Kommunikation - Ja eller Nej?

u

Jeg fryser

JEG HAR SVÆRT VED AT  
NÅ ALARMEN.

Skal du have

Hovedgæret op

ELLER NED?

Skal benenden op  
eller ned?

Tæppet og  
Dynebetrækket må ikke ligge  
stramt om mine Fødder

08>

Skal du tisse?

Har du det for varmt?

Skal jeg vende din dyne?

Skal jeg skifte dynen frem for et  
lagen?

IMELLEN DYNE  
TÆPPE  
SKAL ALARMEN  
JUS  
FOR  
N/A

JOBS NÅR DER SKIFTES

Skal jeg skifte dynen frem for et  
lagen + tæppe?

Skal døren åbnes et par minutter?

Skal dine arme og finger strækkes  
og lægges ovenpå dynen?

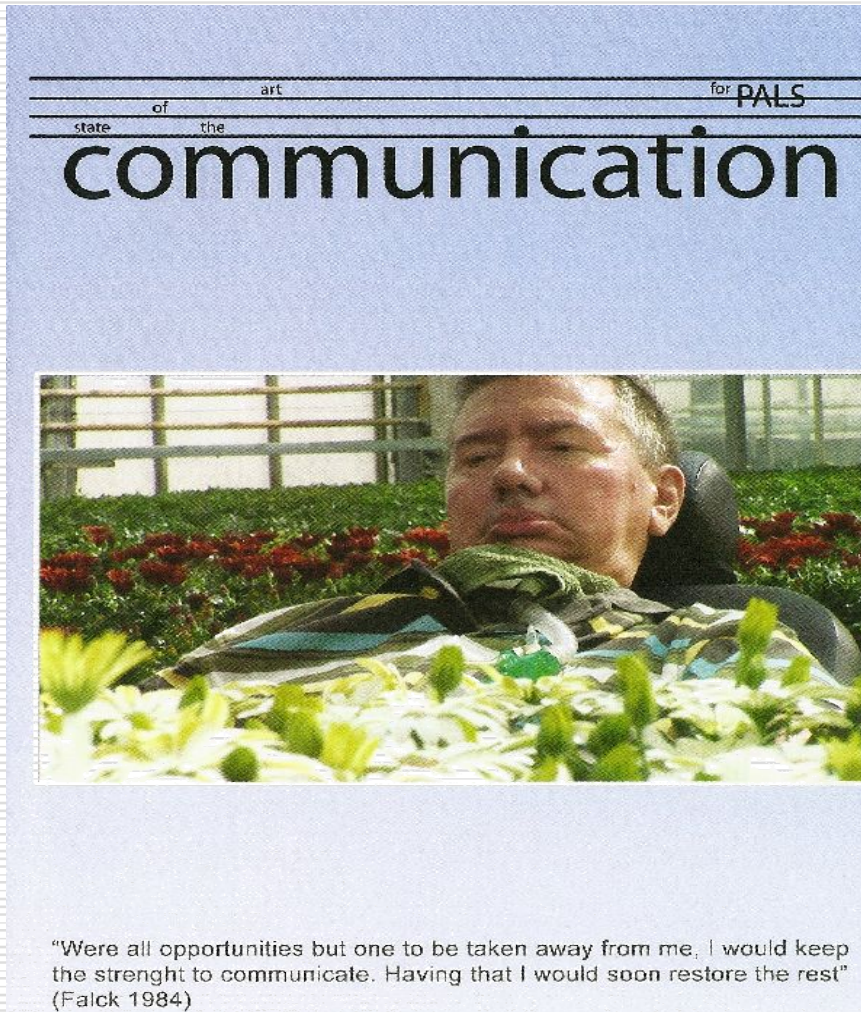
Skal dine arme under dynen?

ALTID DEN TYKKE SIDE PÅ PUDEN



# 7. kommunikation - DVD

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DVD'en kan ses på:

<http://www.als-communication.dk>

# 8: Enteral nutrition in ALS Patients

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1. Bulbar dysfunction and nutritional status, including at least *weight, should be checked at each visit.*
2. The patient and spouse should be referred to a dietician as soon as dysphagia appears. A speech and language therapist can give valuable advice on swallowing techniques.
3. The timing of PEG/PRG is based on an individual approach taking into account bulbar symptoms, malnutrition (weight loss > 10 %), respiratory function and the patient's general condition. *Thus, early operation is highly recommended.*
4. When PEG is indicated, patient and carers should be informed: a) of the benefits and risks of the procedure; b) that it is possible to continue to take food orally as long as it is possible; c) that deferring PEG to a late disease stage may increase the risk of the procedure.
5. Percutaneous Radiologic Gastrostomy (PRG; RIG) is a suitable alternative to PEG. This procedure can be used as the procedure of choice or when the PEG is deemed hazardous
6. Tubes with large diameter should be recommended for both PEG and PRG in order to prevent tube obstruction.
7. Prophylactic medication with antibiotics on the day of the operation may reduce the risk of infections.

# 8. Ernæring – PEG-sonde?

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- Monitore ernæringstilstand (BMI)
- Tidsforbrug og ubehag ved alm. spising
- Fejlsynkning – risiko for lungebetændelse
- Anlæg PEG-sonde i god almen tilstand og forceret vitalkapacitet > 50 %
  - Risiko peritonitis

# 8. Ernæring – Peg-sonde

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Findes der opgørelser i Danmark?

- 1974 - 1986

- 1993 - 1998

- Overlevelse 23 mdr.

- Overlevelse 33 mdr.

- 2% PEG-sonde

- 46% PEG-sonde



# Hvis man ikke kan? – kan man..

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Gå

- Bruge kørestol

Trappegang

- Trappelift

Bruge armene

- Personlig hjælper

Tale

- staveplade

- Øjenstyret PC

Spise

- PEG-sonde

Trække vejret

- BiPAP, respirator  
eller †



# 9: Non-invasive and invasive ventilation (1/2)

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1. **Symptoms or signs of respiratory insufficiency** (including symptoms of nocturnal hypoventilation) **should be checked at each visit.**
2. **VC is the most available and practical** test for the monitoring of respiratory function on a regular basis. If possible, VC should be measured both standing/sitting and lying.
3. **Nocturnal oxymetry**, available at home, is recommended in patients with symptoms of nocturnal hypoventilation.
4. Symptoms or signs of respiratory insufficiency should **initiate discussions** with the patient and the caregivers about all treatment options such as NIV, TV and the terminal phase. Early discussions are needed to allow advance planning and directives.

## 9: Non-invasive and invasive ventilation (2/2)

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1. The patient should **be informed about the temporary nature of NIV** (which is primarily directed towards improving quality of life rather than prolonging it (as opposed to TV)).
6. TV can prolong survival for many months and can improve patient's quality of life, but it has **major impact upon carers**, and be undertaken only after full discussion of the pro's and con's with the patient and carers.
7. **Oxygen therapy** alone should be avoided as it may exacerbate CO<sub>2</sub> retention and mouth dryness.



# 9. Respiration

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- Udspørge og informere om sympt. på natlig hypoventilation
- Monitore forceret vitalkapacitet og peakflow
  
- Informere om resp. hjælpemidler
- Henvise til Respirationscenter Ø el. V.

# 10: Palliative and End-of-Life Care (1/2)

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1. Whenever possible, offer input from a **palliative care** team early in the course of the disease.
2. **Initiate discussions on end-of-life decisions whenever the patient asks – or 'opens the door' – for end-of-life information and/or interventions.**
3. **Discuss the options for respiratory support and end-of-life issues if the patient has dyspnea, other symptoms of hypoventilation, or a forced vital capacity <50%.**
4. Inform the patient of the legal situation regarding advance directives and naming of a health care proxy. Offer assistance in formulating an advance directive.
5. Re-discuss the patient's preferences for life-sustaining treatments every six months.



## 10: Palliative and End-of-Life Care (2/2)

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6. Initiate early **referral to hospice or home care teams** well in advance of the terminal phase of ALS to facilitate the work of the hospice team.
7. Be aware of the importance of **spiritual issues** for the quality of life and treatment choices.
8. For symptomatic treatment of dyspnea and/or pain of intractable cause **use opioids** alone or in combination with **benzodiazepines** if anxiety is present.
9. For treating terminal restlessness and confusion due to hypercapnia **neuroleptics** may be used, chlorpromazine (12,5 mg every 4 to 12 hours i.v.).