
Article:
Baxter, S. orcid.org/0000-0002-6034-5495, Johnson, M. orcid.org/0000-0003-0850-234X, Clowes, M. orcid.org/0000-0002-5582-9946 et al. (7 more authors) (2019) Optimizing the noninvasive ventilation pathway for patients with amyotrophic lateral sclerosis/motor neuron disease: a systematic review. Amyotrophic Lateral Sclerosis & Frontotemporal Degeneration, 20 (7-8). pp. 461-472. ISSN 2167-8421

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Supplementary File

1. Study appraisal checklists

Comparative studies

First author & date	Potential for selection bias?		Potential for performance bias?	Potential for detection bias?	Potential for attrition bias?	Potential reporting bias?	Other
	Random sequence generation.	Allocation concealment.	Blinding of participants and personnel	Blinding of outcome assessments	Incomplete outcome data assessments	Selective reporting.	
Bertella 2014/2017	Yes	Not possible	Not possible	Not possible	No	No	
Jackson 2001	Yes	Not possible	Not possible	Unclear	No	No	Very s
Lopes 2009/2012	Assigned according to residential area	Not possible	Not possible	Not possible	No	Yes	Compl hospit partial
Pinto 2003	No	Not possible	Compared to historic group	Unclear	No	Potentially	
Pinto 2010	No	Not possible	Not possible	Unclear	No	No	
Terzano	No	Not possible	Not possible	Unclear	No	No	
Vrijsen 2017	Yes	Not possible	Not possible	Unclear	No	No	

Cross-sectional studies

First author & date	1. Was the research question clearly stated?	2. Was the study population clearly specified and defined?	3. Was the participation rate of eligible persons at least 50%?	4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study pre-specified and applied uniformly to all participants?	5. Was a sample size justification, power description, or variance and effect estimates provided?	6. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome?	7. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	8. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?
Andersen 2018/Kuzma-Kosakievicz 2016	Y	Y	Unclear	N	N	N/A	N/A	Y
Banerjee 2013	Y	Y	Y	Y	N	N/A	N/A	Y
Chaudri 2000	Y	Y	Y	Y	N	N/A	Y	Y
Chio 2001	Y	Y	N 36 of 80 centres	N	N	N/A	N/A	Y
Cousins, 2013	Y	Y	Y	Y	N	Y	Y	Y
Crescimanno 2016	Y	Y	Y	Y	Y	N/A	Y	Y
Elman 2003	Y	Y	Y	Y	N	N/A	Y	Y
Fantini 2016	Y	Y	Y	Y	N	N	Y	Y
Heiman-Patterson 2017/2018	Y	Y	Unclear	Y	N	N/A	N/A	N/A
Melo 1999	Y	Y	N 20 of 48 centres	Y	N	N/A	N/A	N/A

Nixon 2015/Oliver 2015	Y	Y	Y	Y	N/A	Y	N/A	N/A	N/
O Neil 2012	Y	Y	Unclear	Y	N	N/A	N/A	N/A	N/
Pinto 2017	Y	Y	Y	Y	N	Y	Y	Y	N po
Rafiq 2012	Y	Y	Unclear	Y	N	Y	Y	Y	N po
Ritsma 2009/2010	Y	Y	Unclear	Unclear	N	N/A	N/A	N/A	N/
Ruffell 2012/2013	Y	Y	N 12%	Y	N	N/A	N/A	N/A	N/
Schellas 2018	Y	Y	Y	Y	N	Y	Y	Y	U
Trail 2003	Y	Y	Unclear	Y	N	Y	Y	Y	N
Vitacca 2013	Y	Y	N	Y	N	N/A	N/A	N/A	N/

Cohort (prospective) studies

First author & date	1. Was the study question or objective clearly stated?	2. Were eligibility/selection criteria for the study population pre-specified and clearly described?	3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	4. Were all eligible participants that met the pre-specified entry criteria enrolled?	5. Was the sample size sufficiently large to provide confidence in the findings?	6. Was the test/service/intervention clearly described and delivered consistently across the study population?	7. Were the outcome measures pre-specified, clearly defined, valid, reliable, and assessed consistently across all study participants?	8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?
Bourke 2003	Y	Y	Y	Y	Y	Y	Y	Unclear	Y
Braga 2013 a/b 2017	Y	Y	Y	Unclear	Y	Y	Y	Unclear	Y
Cederbaum 2001	Y	Y	Y	Y	Y	Y	Y	Unclear	Y
Chio 2006	Y	Y	Y	Y	Y	Y	Y	N/A	N/A
Gonzelez-Bermejo 2013	Y	Y	Y	Y	Y	Unclear	Y	Unclear	Y
Gonzalez Calzada 2016	Y	Y	Y	Y	Y	Y	Y	Unclear	N/A
Martin 2014	Y	Y	Y	N	Y	Y	Y	Unclear	N
Martinez 2015	Y	Y	Y	Unclear	Y	Unclear	Y	Unclear	N
McKim 2012	Y	Y	Y	Unclear	Y	Unclear	Y	Unclear	N
Morgan 2005	Y	Y	Y	Unclear	Y	Y	Y	Unclear	N
Sheers 2013/2014	Y	Y	Y	Unclear	Y	Y	Y	Not possible	Unclear
Tamplin 2017	Y	N	Y	N	Y	Unclear	N	N	Y
Vandenberghe 2013	Y	Y	Y	Y	Y	Y	Y	Unclear	N
Volanti 2011	Y	Y	Y	Y	Y	Y	Y	Not possible	Y
Vrijsen 2016	Y	Y	Y	Unclear	Y	Y	Y	Unclear	Unclear
Yamauchi 2013 ab/2014	Y	Y	Y	Unclear	Y	Y	Y	Unclear	N
Martin 2014	Y	Y	Y	Unclear	Y	Y	Y	Not possible	N

Chart review (retrospective studies)

	Well-defined, clearly articulated research question	Sampling questions considered a priori	Operationalize variables included in retrospective chart review	Train and monitor data abstractors	Develop and use standardized data abstraction forms	Create a data abstraction procedure manual	Develop explicit inclusion and exclusion criteria	Address inter-rater and intra-rater reliability	Conduct a pilot test	Address confidentiality and ethical considerations
Bedard 2016	Y	N	Y	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Farrero 2005	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Georges 2016	Y	N	Not reported	Not reported	Not reported	Not reported	y	Not reported	Not reported	Not reported
Gruis 2005/2006	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Jackson 2006	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Khamanker 2018	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Lowewen 2014	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Nicholson 2017	Y	N	Y	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Peysson 2008	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported

Prell 2015/2016	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Sancho 2014	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Stewart 2001	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported
Tilanus 2017	Y	N	Not reported	Not reported	Not reported	Not reported	Y	Not reported	Not reported	Not reported

Quality assessment of qualitative papers

Study	**1**	**2**	**3.**	**4.**	**5**	**6**	**7**	**8.**	**9**	**1**	**Comments**
Ando 2014	Y	Y	Y	CT	Y	N	Y	CT	Y	Y	Same study
Ando 2014	Y	Y	CT	Y	Y	Y	Y	Y	Y	Y	
Baxter et al 2013	Y	Y	CT	Y	Y	N	Y	Y	Y	Y	Same study
Baxter et al 2013	Y	Y	CT	Y	Y	N	Y	Y	Y	Y	
Greenaway et al 2015	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Same study
Martin et al 2016	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	
Faull et al 2013	Y	Y	CT	CT	Y	N	Y	Y	Y	Y	Same study
Phelps et al 2015	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	
Sundling et al 2009	Y	Y	Y	CT	Y	Y	Y	Y	Y	Y	

For each, Yes, Can't Tell or No

1. Was there a clear statement of the aims of the research? (what was the goal of the research; why it was thought important; its relevance)
2. Is a qualitative methodology appropriate? (If the research seeks to interpret or illuminate the actions and/or subjective experiences of research participants; Is qualitative research the right methodology for addressing the research goal)
3. Was the research design appropriate to address the aims of the research? (if the researcher has justified the research design, e.g. have they discussed how they decided which method to use)
4. Was the recruitment strategy appropriate to the aims of the research? (If the researcher has explained how the participants were selected; If they explained why the participants they selected were the most appropriate to provide access to the type of knowledge sought by the study; If there are any discussions around recruitment, e.g. why some people chose not to take part)
5. Was the data collected in a way that addressed the research issue? If the setting for the data collection was justified; If it is clear how data were collected (e.g. focus group, semi-structured interview etc.); If the researcher has justified the methods chosen; If the researcher has made the methods explicit (e.g. for interview method, is there an indication of how interviews are conducted, or did they use a topic guide); If methods were modified during the study. If so, has the researcher explained how and why; If the form of data is clear (e.g. tape recordings, video material, notes etc.); If the researcher has discussed saturation of data
6. Has the relationship between researcher and participants been adequately considered? (If the researcher critically examined their own role, potential bias and influence during (a) formulation of the research questions (b) data collection, including sample recruitment and

choice of location; How the researcher responded to events during the study and whether they considered the implications of any changes in the research design

7. Have ethical issues been taken into consideration? (If there are sufficient details of how the research was explained to participants for the reader to assess whether ethical standards were maintained; If the researcher has discussed issues raised by the study (e.g. issues around informed consent or confidentiality or how they have handled the effects of the study on the participants during and after the study; If approval has been sought from the ethics committee
8. Was the data analysis sufficiently rigorous? (If there is an in-depth description of the analysis process; If thematic analysis is used. If so, is it clear how the categories/themes were derived from the data; Whether the researcher explains how the data presented were selected from the original sample to demonstrate the analysis process; If sufficient data are presented to support the findings; To what extent contradictory data are taken into account; Whether the researcher critically examined their own role, potential bias and influence during analysis and selection of data for presentation
9. Is there a clear statement of findings? (If the findings are explicit; If there is adequate discussion of the evidence both for and against the researcher's arguments; If the researcher has discussed the credibility of their findings (e.g. triangulation, respondent validation, more than one analyst); If the findings are discussed in relation to the original research question
10. How valuable is the research? (if the researcher discusses the contribution the study makes to existing knowledge or understanding (e.g. do they consider the findings in relation to current practice or policy, or relevant research-based literature; If they identify new areas where research is necessary; If the researchers have discussed whether or how the findings can be transferred to other populations or considered other ways the research may be used

2. List of studies excluded at full paper screening

1. Al-Chalabi A. The multidisciplinary clinic, quality of life and survival in motor neuron disease. Journal of Neurology 2007;254:1118.	Data not related specifically to NIV
2. Bach JR, Bianchi C, Aufiero E. Oximetry and indications for tracheotomy for amyotrophic lateral sclerosis. Chest 2004;126:1502-1507.	Data unrelated to optimal use
3. Berrube L, Declercq PL, Lamia B, Muir JF, Cuvelier A. Long-term adherence to domiciliary NIV and its relation to survival in patients with chronic respiratory failure. European Respiratory Journal 2013;42.	Reports effects of NIV
4. Boentert M, Brenscheidt I, Glatz C, Young P. Effects of non-invasive ventilation on objective sleep and nocturnal respiration in patients with amyotrophic lateral sclerosis. Journal of neurology 2015;262:2073-2082.	Reports effects of NIV
5. Bourke SC, Tomlinson M, Williams TL, Bullock RE, Gibson GJ, Shaw PJ. A randomised controlled trial of non-invasive ventilation (NIV) in motor neurone disease (MNC). Journal of Neurology Neurosurgery and Psychiatry 2006;77:136-137.	Reports effects of NIV
6. Braga AC, Pinto A. Health Care Management in ALS Patients. Home Health Care Management & Practice 2015;27:201-207.	Explores effects on a variety of management interventions on quality of life
7. Brylev L, Byalik M, Chervyakov A, et al. Home-based multidisciplinary care for ALS/MND in Moscow and Russia. Journal of Neuromuscular Diseases 2014;1:S344-S345.	Describes features of ALS patients in Russia
8. Calero K, Elamin E, Anderson WM. Targeting subgroups of patients with ALS: A step towards individualized therapy. Sleep 2015;38:A284-A285.	Compares usage of NIV and tracheostomy in cervical and bulbar patients
9. Chio A, Ilardi A, Cammarosano S, Moglia C, Montuschi A, Calvo A. Neurobehavioral dysfunction in ALS has a negative effect on outcome and use of PEG and NIV. Neurology 2012;78:1085-1089.	Explores the effect of neurobehavioural dysfunction on outcomes
10. Green B, Adeniji K, Wilkinson J. Non-invasive ventilation in motor neuron disease: An audit of current practice. Thorax 2007;62:A9-A9.	Conference abstract unable to source
11. Nottingham University Hospitals. Guidelines for Caring for patients requiring non-invasive ventilation via Nippy S+ ventilator. Nottingham:	Not MND-specific, unable to isolate information relating to MND

Nottingham University Hospitals, 2016.	
12. Agency for Clinical Innovation. Non-invasive Ventilation Guidelines for Adult Patients with Acute Respiratory Failure. Chatswood: New South Wales Government, 2014.	Not MND-specific, unable to isolate information relating to MND
13. Kleopa KA, Sherman M, Neal B, Romano GJ, Heiman-Patterson T. Bipap improves survival and rate of pulmonary function decline in patients with ALS. Journal of the neurological sciences 1999;164:82-88.	Reports effects of NIV
14. Kuleci S, Koc F, Hanta I. Profile of Respiratory Impairment in Patients With Amyotrophic Lateral Sclerosis at Initial Admittance. Neurosurgery Quarterly 2010;20:288-291.	Reports levels of respiratory impairment
15. Meyer T, Dullinger JS, Munch C, et al. [Elective termination of respiratory therapy in amyotrophic lateral sclerosis]. Elektive Termination der Beatmungstherapie bei der amyotrophen Lateralsklerose 2008;79:684-690.	Termination of all types of ventilation
16. Morelot-Panzini C, Perez T, Gilet H, et al. Dyspnea as the major driver of anxiety in amyotrophic lateral sclerosis. European Respiratory Journal 2014;44.	Evaluates use of the multimensional dyspnea profile
17. Mustfa N, Walsh E, Bryant V, et al. The effect of noninvasive ventilation on ALS patients and their caregivers. Neurology 2006;66:1211-1217.	Reports effects of NIV on quality of life with no data relating to recommendations
18. Park D, Lee GJ, Kim HY, Ryu JS. Different characteristics of ventilator application between tracheostomy- and noninvasive positive pressure ventilation patients with amyotrophic lateral sclerosis. Medicine 2017;96:e6251.	Explores associations between ventilator settings and body weight
19. Sanjuan-Lopez P, Valino-Lopez P, Ricoy-Gabaldon J, Verea-Hernando H. Amyotrophic lateral sclerosis: impact of pulmonary follow-up and mechanical ventilation on survival. A study of 114 cases. Archivos de bronconeumologia 2014;50:509-513.	Reports effects of NIV
20. Schwarz JK, Del Bene ML. Withdrawing ventilator support for a home-based amyotrophic lateral sclerosis patient: a case study. The Journal of clinical ethics 2004;15:282-290.	Invasive ventilation, descriptive overview
21. Servera E, Sancho J, Banuls P, Marin J. Bulbar impairment score predicts noninvasive	Explores factors influencing lower respiratory tract infections in patients

volume-cycled ventilation failure during an acute lower respiratory tract infection in ALS. Journal of the neurological sciences 2015;358:87-91.	with acute respiratory failure
22. Sheers N, Howard ME, Berlowitz DJ. Ambulatory adaptation of non-invasive ventilation in Motor Neuron Disease: Where limits of effectiveness end. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 2015;16:139-140.	Letter to the editor, no data
23. Shtabnitskiy V, Brylev L. Non-invasive ventilation for ALS with respiratory failure in home care settings. European Respiratory Journal 2013;42.	Explores factors relating to risk of death in ALS patients
24. Sloan RH. Use of external nasal dilator strips in motor neurone disease with upper airways obstruction. Palliative Medicine 1999;13:443-443.	Not specifically relating to NIV provision
25. Stewart H, Eisen A, Weber M, Road J. Asymptomatic respiratory muscle denervation: An indication for commencing BiPAP in amyotrophic lateral sclerosis. Neurology 2001;56:A199-A199.	Unable to source
26. Vitacca M, Grassi M, Barbano L, et al. Last 3 months of life in home-ventilated patients: the family perception. Eur Respir J 2010;35:1064-1071.	Describes characteristics of patients, carers and social context, describes use of NIV but no specific data
27. Vrijsen B, Buyse B, Belge C, et al. Noninvasive ventilation improves sleep in amyotrophic lateral sclerosis: a prospective polysomnographic study. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine 2015;11:559-566.	Reports effects of NIV
28. Vrijsen B, Buyse B, Belge C, Testelmans D. Upper airway obstruction during noninvasive ventilation induced by the use of an oronasal mask. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine 2014;10:1033-1035.	Case study of a patient in intensive care
29. Wight AG, Bennett J, Ward K, et al. Improving the patient journey for patients referred for niv in motor neurone disease: Early impact of national guidance. American Journal of Respiratory and Critical Care Medicine 2012;185.	Compares service delivery data to established guidance

3. Individual study extractions

Quantitative and mixed method paper extractions

Agrafiotis, 2017
Journal paper / conference abstract
Country: Greece

RCT	
Non-RCT	
CBA	
BA	
Comparator: None	
Length of follow up: Unclear	
Mixed method	
Cross-sectional	
Other (specify)	Case study

Aim of study: To describe the use of mouthpiece ventilation with cough augmentation to avoid tracheostomy
Data collection method: Pre and post test results
Sample size: 1
Identification/recruitment: Not reported

Participant characteristics:

Condition	ALS ALSFRS score 28
Onset	Limb weakness, non-bulbar, rapid decline of motor and respiratory function
Sex	Male
Age	62
NIV usage	Used only during sleep, progressed to up to 18 hours per day
Other (specify)	

Measures

- Chest radiography
- Arterial blood gases
- Spirometry
- Maximum inspiratory mouth pressure
- Sniff nasal inspiratory pressure
- Peak cough flow
- Use of axillary inspiratory muscles
- Oximetry
- Hours usage

Data relating to NIV provision and usage:
Three months after provision of BPAP he had deteriorated physically considerably. Blood gases were unchanged but FVC, SNIP and PCF had declined. He was severely breathless, used axillary muscles during time off-ventilator, and reported difficulty controlling sputum. He had developed a pressure ulcer on his nose.
A significant improvement in symptoms was achieved following adjustment of the ventilator and replacement of the mask by the mouthpiece. The oro-nasal interface continued to be used at night.
The “air stacking” manoeuvre was also taught to the patient.
Patients should have the ability to grab the mouthpiece with their lips and perform air stacking manoeuvres, it therefore may not be suitable for those with facial muscle weakness or severe bulbar symptoms.
Many practitioners consider transition to tracheostomy when the number of hours per day of ventilator use exceeds an arbitrarily

	Details of technology/NIV Bi level noninvasive ventilation via oronasal mask, also treated with antibiotics. Inspiratory positive airway pressure of 6cm H_2O and back up rate of 16 breaths per minute. The oronasal interface was changed to an angled 15 mm mouthpiece, and assist volume control to deliver a tidal volume of 0.9 with inspiratory time of 1.3 seconds, a square flow wave form, zero PEEP, back up rate of 14 breaths per minute, some obtrusive alarms were de-activated. Patient controlled the number of breaths required and the leak, and placing of mouthpiece.	defined threshold such as 16-20 hours. **Author conclusions:** High levels of usage of noninvasive ventilation is not suitable due to difficulties in eating, drinking, talking, claustrophobia and limited field of vision. The use of a mouthpiece interface during daytime combined with mask ventilation during sleep provides an alternative option to tracheostomy.

Andersen 2012, 2007, 2005
Journal paper / conference abstract
Country: Across countries

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Systematic review

Aim of study: To review literature on the diagnosis and management of ALS
Data collection method: Review of literature and clinical consensus
Sample size: N/A
Identification/recruitment: N/A

Participant characteristics:

Condition	ALS
Onset	
Sex	
Age	
NIV usage	
Other (specify)	

Measures

N/A

Details of technology/NIV

N/A

Data relating to NIV provision and usage:
Specialised multidisciplinary clinics can provide optimised management services with increased use of NIV.
Patients should be reviewed every 2-3 months, although this varies with stage and severity of disease.
There should be effective channels of communication between hospital and community and palliative care teams.
Erect forced vital capacity and vital capacity tests should be performed regularly. SNP may be more accurate for those with weak lips, but is not accurate for those with bulbar involvement (neither is FVC).
Nocturnal oximetry can be useful to determine the need for NIV. Phrenic nerve responses may predict hypoventilation.
There is no clear evidence regarding the timing of NIV or criteria for usage. Treatment is usually initiated at night. Patients with bulbar palsy are less compliant. NIV should be considered in preference to invasive ventilation.
Parenteral morphine, a benzodiazepine and an anti-emetic are used when the patient decides ventilator support should be withdrawn.
Active management of secretions and cough-assist devices is beneficial.
Options for respiratory support and

		end of life issues should be discussed if the patient has dyspnoea, other symptoms of hypoventilation or a FVC below 50%. There should be re-discussion regarding life sustaining treatments every 6 months. **Author conclusions:** Outlined above.

Ando, 2016
Journal paper / **<u>conference abstract</u>**
Country: Unclear

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Cohort

Aim of study: To explore the use of telemonitoring
Data collection method: Data collected weekly
Sample size: 13
Identification/recruitment: Not reported

Participant characteristics:

Condition	MND/ALS
Onset	Not reported
Sex	Not reported
Age	Mean age 62
NIV usage	
Other (specify)	Median illness duration 14 months, median NIV use 8 months

Measures

Nocturnal pulse oximetry
Patient ventilator interaction data

Details of technology/NIV

None

Data relating to NIV provision and usage:
137 alerts were triggered over the 6 month period. There were 13 direct reviews, 14 required treatment adjustment, 20 required change to equipment, and 15 required further referral.
Inspiratory positive airway pressure levels increased, although there was no change in nocturnal SpO2 levels. NIV adherence increased over time.

Author conclusions:
Telemonitoring is beneficial in provision of NIV.

Armstrong, 2010
Journal paper / conference abstract
Country: USA

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Cohort

Aim of study: Explore the role of the nurse co-ordinator in NIV provision
Data collection method: Data from NIV devices collected at least three-monthly
Sample size: Unclear
Identification/recruitment: Not reported

Participant characteristics:

Type of group	
Condition	ALS
Onset	Not reported
Sex	Not reported
Age	Not reported
NIV usage	Not reported
Other (specify)	

Measures

Description of therapy decisions

Details of technology/NIV

Not reported

Data relating to NIV provision and usage:
Monitoring of compliance and efficacy data is useful and should be done every three months as a minimum.

Author conclusions:
Patients may benefit from monitoring of data from NIV machines.

Ashcroft 2015
Journal paper / conference abstract
Country: UK

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	X
Other (specify)	Delphi approach

Participant characteristics:

Condition	MND
Onset	Not reported
Sex	7 male
Age	Mean 62
NIV usage	
Other (specify)	

Measures

Number of alerts
Number of interventions

Details of technology/NIV

Data relating to NIV provision and usage:
210 alerts were triggered, requiring 34 interventions. Median number of interventions was 2 per patient.
The questions developed appeared to be valid to allow appropriate and timely treatment adjustment.

Author conclusions:
There is value in following patients up more frequently than the 3 months recommended in current guidance.
The use of validated questions

<table>
<tr>
<td>Aim of study: To develop questions for patients to complete while using telemonitoring of NIV
Data collection method: Patient report weekly
Sample size: 10 patients
Identification/recruitment: Not reported</td>
<td>Not reported</td>
<td>during telemonitoring offers a useful approach to following up patients.</td>
</tr>
<tr>
<td>Atkeson 2011 a/b
<u>Journal paper / conference abstract</u>
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To study use of nocturnal NIV
Data collection method: Machine readings
Sample size: 23 patients (19 included in analysis)
Identification/recruitment: Consecutively recruited</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>37% predominantly limb, 58% bulbar, 5% repiratory</td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td>At least 4 hours per night on at least 6 nights per week, mean 8.4 hours</td></tr>
<tr><td>Other (specify)</td><td>Seated or supine FVC less than 50% of predicted or orthopnea</td></tr>
</table>
Measures
Polysomnography – airway flow and ventilator pressure delivery
FVC via mouthpiece with nasal clip or mask attached to the spirometer circuit for those with bulbar symptoms.
Finger pulse oximetry
Patient self-reported/carer reported adherence
Patient-ventilator asynchrony index calculated as number of episodes per hour (central apnea in the presence of a ventilator backup rate, non-triggered patient effort – respiratory effort without ventilator assist, out-of-phase patient effort/ventilator assist, or ineffective triggering).</td>
<td>Data relating to NIV provision and usage:
Ventilatory parameters of nNIV including inspiratory and expiratory pressure, backup rate, trigger sensitivity, maximal inspiratory time, and type of interface were set in the patient’s home by respiratory therapists according to awake efficacy of patient ventilator synchrony, patient tolerance and comfort, and awake oxygen saturation of haemoglobin (SpO2) levels of 90% or above as per usual clinical practice. Adjustments of NIVparameters were made according to patient reports of discomfort, air leak, or lack of efficacy.
ing to patient reports of discomfort, air leak, or lack of efficacy.
High frequency of patient-ventilator asynchrony found. Mean AI per hour was 69 +/-46 SD range 15–146). Mean asynchrony time as a percent of recording time was17% +/- 19%.
Percentage time in asynchrony and oxygen desaturation indices did not appear to be appropriate predictors</td>
</tr>
</table>

<table>
<tr>
<td></td>
<td>Oxygen desaturation index

Details of technology/NIV
ResMed VPAP ST III bilevel PAP unit
Type of interface included nasal pillows in 8 patients, a nasal mask in 3 patients, a full face mask in 4 patients, and a hybrid interface (mouthpiece with nasal pillows) in 2 patients.</td>
<td>of asynchrony severity.
No association found between measures of ALS severity and asynchrony.
Patients with predominantly bulbar ALS tended to show a lower frequency of nocturnal oxygen desaturation episodes with nNIV in contrast to expectations.

Author conclusions: Current practice of nNIV use is not likely to be providing optimal nocturnal ventilatory support in patients with ALS.</td>
</tr>
<tr>
<td>Banerjee 2013
<u>Journal paper (letter)</u> / conference abstract
Country: UK
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td>X</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Aim of study: To compare mask and tube interfaces for spirometry
Data collection method: Spirometry reading
Sample size: 60
Identification/recruitment: Consecutive patients</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS mean ALSRFRS score 7.8</td></tr><tr><td>Onset</td><td></td></tr><tr><td>Sex</td><td></td></tr><tr><td>Age</td><td>Mean 64.7</td></tr><tr><td>NIV usage</td><td>Not reported</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
FVC via spirometer
PiMax
SNIP

Details of technology/NIV
A calibrated hand-held spirometer via a tube or a face mask (Leardal, child No.4)</td>
<td>Data relating to NIV provision and usage:
Mask preferred by 44 patients.
Successful measurement was achieved for all patients using mask spirometry, and for 54 using tube spirometry. Using SNIP and PiMax measurements from 45 patients were obtained. The mask gave significantly greater values than the other measurement approaches.

Author conclusions: Mask spirometry achieves better results than other interfaces.</td>
</tr>
</table>

Bannerjee 2011
Journal paper / conference abstract
Country: UK

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Review of data

Aim of study: To evaluate introduction of a respiratory care unit
Data collection method: Routine data 1984-2010
Sample size: Unclear
Identification/recruitment: All those referred

Participant characteristics:

Type of group	Patients
Condition	ALS
Onset	Not reported
Sex	Not reported
Age	Not reported
NIV usage	Not reported
Other (specify)	

Measures

Referrals
Use of NIv

Details of technology/NIV

From 2006 the default position was to offer all patients newly diagnosed with MND a respiratory assessment and structured 3 monthly follow-up appointments

Data relating to NIV provision and usage:
Between 1984 and 2000 there was slow growth but the mean annual values were just seven referrals and four new NIV starters (57%). With closer working between neurologists in the care centre and the respiratory unit between 2001 and 2005 mean referral numbers increased to 31 with 17 new NIV starters (55%) per year.

Author conclusions:
Following establishment of regional respiratory unit and care centre increased referral and offering NIV

Barthlen 2000
Journal paper / conference abstract
Country: USA

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Case studies

Participant characteristics:

Measures

FVC

Type of group	Patients
Condition	ALS
Onset	Unspecified
Sex	Male
Age	61 and 56
NIV usage	Prior to initiation
Other (specify)	

Details of technology/NIV

Not reported

Data relating to NIV provision and usage:
On assessment both patients had severe sleep maintenance insomnia with sleep efficiency of less than 40% and frequent disturbance, despite little report of nocturnal problems.

Author conclusions: Patients with minimal weakness but who have other vague symptoms of daytime sleepiness may have severe

<table>
<tr>
<td>Aim of study: To present 2 case studies
Data collection method:
Sample size: 2
Identification/recruitment: Not reported</td>
<td></td>
<td>respiratory de-saturations and should undergo polysomnography.</td>
</tr>
<tr>
<td>Bedard 2016
<u>Journal paper</u> / conference abstract
Country: Canada
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Retrospective chart review</td></tr>
</table>
Aim of study: To explore the use and outcomes of daytime mouthpiece ventilation added to night time mask ventilation
Data collection method:
Sample size: 37
Identification/recruitment: unclear</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>Probable or definite ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td>24 more than 12 hours daily NIV use 5 had less than 12 hours of daytime use</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
FVC
Maximum inspiratory pressure
Maximum expiratory pressure
Maximum voluntary ventilation,
Maximum insufflation capacity.
Peak cough flow

Details of technology/NIV</td>
<td>Data relating to NIV provision and usage:
6 of 37 were unable to use mouthpiece ventilation. Two preferred to use a mask, four were unable to use it adequately.
Indications for nocturnal NIV included orthopnea, daytime hypercapnia, symptoms of sleep-disordered breathing, FVC >50% of predicted, or maximum inspiratory pressure <40 cm H2O.
When NIV use is >12 h/ day, mouthpiece ventilation is recommended for those who wish to pursue 24-h NIV and who maintain sufficient bulbar function to retain a mouthpiece and achieve an adequate seal around it in order to maintain adequate ventilation and perform lung-volume recruitment.
Patients completed respiratory assessments and pulmonary function testing every 2–6 months, depending on the rate of progression.
Patient education included a session on respiratory care, NIV, and advance directives. For mouthpiece ventilation an out patient education session was held with a trial and adjustment.</td>
</tr>
</table>

	Ventilator tubing and mouthpiece are mounted on the wheelchair Continuous mandatory ventilation mode is used. Tidal volume (from 800 to 1,800 mL), inspiratory time, and breathing frequency were set according to the subject's need and comfort. The second ventilator is used in pressure-control,mode with previous nighttime parameters and replaces the bi-level device.		Adjustments were made based on comfort, symptoms, and downloaded bi-level data, carbon dioxide level, and overnight oximetry. Thirty-one subjects were successful with mouthpiece ventilation, 2 stopped because of lack of motivation, and 4 with bulbar symptoms failed to use it consistently. Thirty of the successful subjects were able to generate a maximum insufflation capacity vital capacity difference with lung volume recruitment **Author conclusions:** Mouthpiece ventilation provides effective ventilation for those requiring full time ventilation and without substantial bulbar involvement as an alternative to tracheostomy. Mouthpiece ventilation should be offered as an alternative to tracheostomy for individuals able to hold a mouthpiece, protect the airway, and assist cough flows for airway clearance. The b-ALFSRFS-Rscore seems to be a simple and useful tool to assess candidacy for mouthpiece ventilation.
Belchior 2012 **Journal paper / conference abstract** **Country:** Portugal **RCT** **Non-RCT** **CBA**	**Participant characteristics:** **Type of group**: Patients **Condition**: 3 with ALS **Onset**: Unclear **Sex**: 2 male **Age**: 62, 69, 70		**Data relating to NIV provision and usage:** First patient had nasal bridge sores from oronasal masks, and several models of interface were tried to improve tolerance; however, one patient did not tolerate any kind of

<table>
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<table>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Case studies</td></tr>
</table>
Aim of study: To report the use of total face masks
Data collection method: Descriptive data
Sample size: 4 (three ALS)
Identification/recruitment: Unclear
</td>
<td>
<table>
<tr><td>NIV usage</td><td>Continuous</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table>
<tr><td>Use of mask</td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>Smaller model of a total face mask that covers the entire face (PerforMax, Philips Respironics, Murrysville, Penn-sylvania)</td></tr>
</table>
</td>
<td>nasal pillows and could not adapt to a mouthpiece with and without lip seal, due to lack of oral sensitivity and anxiety. She was then introduced to a total face mask model that, having no contact with the nose, immediately improved the patient’s comfort and tolerance. A second patient used NIV continuously and developed nasal bridge sores. He developed severe bulbar weakness and tracheostomy was proposed. Adaption to a total face mask was immediate, although a tracheostomy was later performed. The third patient used NIV continuously but with poor tolerance and difficulties with secretion management. A full face mask was proposed as an interim measure while decision-making regarding tracheostomy was made.
Author conclusions: The PerforMax total face mask is a useful and effective interface for patients who do not tolerate a nasal or oronasal mask.</td>
</tr>
<tr>
<td>
Bertella 2014/2017
<u>Journal paper</u> / <u>conference abstract</u>
Country: Italy
<table>
<tr><td>RCT</td><td>X</td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator: In patient versus out patient</td></tr>
</table>
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
</td>
<td>Data relating to NIV provision and usage:
There were no differences in acceptance failure (P=0.733) or adherence failure (P=0.529) between groups initiated in the different locations. At baseline, outpatients had longer hours of nocturnal ventilation (P<0.02) however, at follow up this was similar (P=0.34). Female gender</td>
</tr>
</table>

Length of follow up: 3 months **Mixed method** **Cross-sectional** **Other (specify)** **Aim of study:** To explore whether the location of initiation predicts acceptance and use **Data collection method:** Respiratory function tests, gas analysis, sleep study **Sample size: 50** **Identification/recruitment:** Those referred to a clinic were randomised	FVC Forced expiratory volume at 1st second (FEV1), FEV1/FVC, MIP and maximal expiratory pressure (MEP), Total lung capacity Slow vital capacity Arterial blood gases analysis Mean peripheral oxygen saturation, Oxygen desaturation index Apnea/hypopnea index Time with SpO2<90% (by means of Embletta Z10 System cardio-respiratory monitoring, Med Care Flaga, Reykjavik). Sleep quality scale Patient acceptance Symptoms scale Patient experience Staff experience Patient adherence Details of technology/NIV Pressure-support ventilators (Trend II ST 30, Hoffrichter, Schwerin, Germany, or BiPAP Synchrony II, Philips Respironics, Murrysville, PA, USA) in spontaneous/timed mode with a preset tidal volume (300 mL/kg) and a fixed back-up respiratory rate (12 breaths/min). The NIV trial included: choice of the best fitting facial mask, setting of inspiratory pressure to maximal patient comfort, variable expiratory pressure according to AHI. Direct supervision of a respiratory physician and physiotherapist. The in-hospital care lasted at least 4 hours/day, then the trial proceeded at home during the night. Educational sessions were provided during the		and spinal onset of the disease were predictors for NIV acceptance/adherence failure. The health professionals involved indicated similar satisfaction for both settings of NIV initiation (7.12±2.77 for outpatients vs. 7.05±2.09 for inpatients; P=0.93). The time required for adaption for inpatients group (hospital length of stay) was 10±3 days, while the number of outpatient sessions for the outpatient group was 4±2 during a time course of 15±4 days. **Author conclusions:** Early outpatient initiation of NIV in ALS is as effective as inpatient initiation.

<table>
<tr>
<td></td>
<td>initiation period to each patient in order to ensure that
NIV use was adequate and the ventilator well managed (max. 10 sessions/patient).
Patients were recommended to use nocturnal NIV as much as possible until they had completely adapted to the therapy.</td>
<td></td>
</tr>
<tr>
<td>Bommireddipalli 2017
Journal paper / <u>conference abstract</u>
Country:USA
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr><tr><td>Other (specify)</td><td>Retrospective cohort</td></tr></table>Aim of study: To compare MIP versus FVC measurements
Data collection method: Data collected at clinic visits
Sample size: 264
Identification/recruitment: On clinic visit</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td></td></tr><tr><td>Condition</td><td></td></tr><tr><td>Onset</td><td></td></tr><tr><td>Sex</td><td></td></tr><tr><td>Age</td><td></td></tr><tr><td>NIV usage</td><td></td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
FVC

Details of technology/NIV
Unclear</td>
<td>Data relating to NIV provision and usage:
Older female patients with greater proportion of bulbar disease and faster pre-diagnosis progression rate, are likely to present at time of diagnosis meeting criteria for NIV by MIP, independent of FVC

Author conclusions:
MIP is an early, sensitive indicator for initiation of NIV.</td>
</tr>
<tr>
<td>Bourke 2003
<u>Journal paper</u> / conference abstract
Country: UK
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr></table></td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td></td></tr><tr><td>Sex</td><td></td></tr><tr><td>Age</td><td></td></tr><tr><td>NIV usage</td><td>15 accepted NIV,</td></tr></table></td>
<td>Data relating to NIV provision and usage:
Survival and duration of QoL benefit were strongly related to NIV compliance.
Orthopnea was the best predictor of benefit from, and compliance with,</td>
</tr>
</table>

Comparator: **Length of follow up:** 26 months or death **Mixed method** | **Cross-sectional** | **Other (specify)** | **Cohort** **Aim of study:** To evaluate criteria for initiating treatment **Data collection method:** Clinical tests **Sample size:** 17 **Identification/recruitment:** Consecutive	Measures QoL (Short Form-36 [SF-36], Chronic Respiratory Disease Questionnaire, Sleep Apnea Quality of Life Index) Respiratory function tests every 2 months Polysomnography every 4 months Details of technology/NIV Not provided		10 continued use **Other (specify)** Orthopnea, daytime sleepiness, unrefreshing sleep, daytime hypercapnia, nocturnal desaturation, or an apnea-hypopnea index (AHI) of >10.	NIV. Daytime hypercapnia and nocturnal desaturation also predicted benefit but were less sensitive. Sleep-related symptoms were less specific, and AHI > 10 was unhelpful in predicting compliance/benefit. Moderate or severe bulbar weakness was associated with lower compliance and less improvement in QoL **Author conclusions**: Patients with orthopnea and preserved bulbar function showed the largest benefit.
Braga 2013 a/b 2017 **Journal paper / conference abstract** **Country: Portugal**	**Participant characteristics:**	**Type of group** | Patients **Condition** | Probable or		**Data relating to NIV provision and usage:** Data from NIV settings was

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up: 5 years	
Mixed method	
Cross-sectional	
Other (specify)	**Cohort**

Aim of study: To examine the effect of settings on outcomes.
Data collection method: Data from machines collected every 3 months
Sample size: 60
Identification/recruitment:

Measures

NPO measured by fingertip infra-red pulse oximeter
Mean oxygen saturation overnight
Time in which oxygen saturation was below 90%
Pulmonary function test
FVC (<75%FVC)
MIP
MEP
Compliance

Details of technology/NIV

Ventilated based on results of nocturnal pulsed oximetry.

	definitive ALS
Onset	Majority spinal
Sex	43 males, 17 females
Age	
NIV usage	
Other (specify)	

associated with the rate of functional decline (EPAP. IPAP and backup breath rate, MIP-PFT and $Sp0_{2\ mean}$).

Author conclusions: The usual criteria of 4 hours per day usage is not sufficient. Analysis of compliance data and ventilator settings is important, with elements affecting respiratory comfort of patients underpinning compliance, with individualised clinical management.

<table>
<tr>
<td></td>
<td>Bipap Goodknight 425-ST bi level device
Rehabilitation physician</td>
<td></td>
</tr>
<tr>
<td>Burden 2016
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Retrospective analysis of clinic notes comparing prior to the clinic and after</td></tr>
</table>
Aim of study: To evaluate a new joint palliative and respiratory clinic
Data collection method: Case note analysis
Sample size: 26
Identification/recruitment: Via clinic</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>45% female in joint clinic group</td></tr>
<tr><td>Age</td><td>Mean age 69 in joint clinic group</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td>With respiratory symptoms</td></tr>
</table>
Measures
Number of referrals
Admissions
Deaths
Access to palliative services

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
80% of patients pre-joint clinic were referred to palliative care, compared to 100% following the introduction of the clinic.
80% of patients were initiated on NIV in the standard group compared to 45% in the joint clinic group. (These data appear to be reported in error)

Author conclusions: Patients with MND may benefit from a combined palliative and respiratory joint clinic when making decisions around NIV.</td>
</tr>
<tr>
<td>Buttle 2015
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
</table></td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
</table></td>
<td>Data relating to NIV provision and usage:
There was no significant change in IPAP (Mean 14.78 at 1 month, 14.98 at 3 months) or EPAP (5.91 at 1 month, 6.57 at 3 months).</td>
</tr>
</table>

BA		**NIV usage**	6-8 hours	Average use (6 hrs 44 min at one month increased to 8 hrs 48 min at three months) and compliance (percent greater than 4 h 77.6% at 1 month) increased to 89.5% at 3 months but the change did not reach significance.
Comparator:		**Other (specify)**		
Length of follow up:				
Mixed method				
Cross-sectional				
Other (specify)	Retrospective case note review			
Aim of study: To assess the potential benefits of average volume-assured pressure support in the delivery of NIV. **Data collection method:** Data from case notes and machines **Sample size: 6** **Identification/recruitment:** Unclear		**Measures** IPAP EPAP Average use **Details of technology/NIV** Not reported		**Author conclusions:** Initial data suggest no benefit in providing the more expensive AVAPS machine compared to standard BiPAP S/T mode.
Carrutu 2016 **Journal paper** / **conference abstract** **Country:** Unclear		**Participant characteristics:**		**Data relating to NIV provision and usage:** A statistical negative correlation was found between SNIP and PaCO2 (N=22, p=0.042, r=-043), while FVC did not correlate (N=22, p=0.093, r=-0.36) SNIP negatively correlated to AHI (N=22, p=0.03, r=-0.41), while FVC did not correlate (N=22, p=0.08, r=-0.38). There was also a positive correlation between SNIP and total sleep time (N=22, p=0.03, r=0.7), but not for FVC. **Author conclusions**: a SNIP test, which is non-invasive and easy to
RCT		**Type of group**	Patients	
Non-RCT		**Condition**	ALS	
CBA		**Onset**	Not reported	
BA		**Sex**	Not reported	
Comparator:		**Age**	Not reported	
Length of follow up:		**NIV usage**	Not reported	
Mixed method		**Other (specify)**		
Cross-sectional	X			
Other (specify)				
Aim of study: To evaluate the features of a range of pulmonary function tests **Data collection method:** Pulmonary		**Measures** Apnea Oxygen saturation Total sleep time **Details of technology/NIV** Not reported		

<table>
<tr>
<td>function tests
Sample size: 22
Identification/recruitment: Not reported</td>
<td></td>
<td>reproduce, may early disclose respiratory insufficiency</td>
</tr>
<tr>
<td>Carver 2012
Journal paper / <u>conference abstract</u>
Country: UK
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr><tr><td>Other (specify)</td><td>Review of cases</td></tr></table>Aim of study: To evaluate changes since introduction of a MDT
Data collection method: Unclear
Sample size: 65
Identification/recruitment: All patients seen in clinic</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>MND</td></tr><tr><td>Onset</td><td>Not reported</td></tr><tr><td>Sex</td><td>Not reported</td></tr><tr><td>Age</td><td>Not reported</td></tr><tr><td>NIV usage</td><td>Not reported</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
Unclear

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
Reports that the number of patients managed by the team which included a respiratory physician had increased and the service has a well-established domiciliary ventilation service.

Author conclusions:
Suggests that increase in patients managed reflects the need for teams closer to home, leading to better access to specialist intervention such as NIV.</td>
</tr>
<tr>
<td>Cazolli 2010/2014
Journal paper / <u>conference abstract</u>
Country: USA
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr></table></td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>MND/ALS</td></tr><tr><td>Onset</td><td>13% respiratory, 56% non bulbar</td></tr><tr><td>Sex</td><td></td></tr><tr><td>Age</td><td></td></tr><tr><td>NIV usage</td><td></td></tr><tr><td>Other (specify)</td><td>26% began NIV during emergency hospitalisation while waiting for</td></tr></table></td>
<td>Data relating to NIV provision and usage:
Patients withdrew from NIV anticipating death to occur as they desired
Some patients were given morphine sulphate at a hospice and became intolerant of NIV
Author conclusions:
Factors independent of excessive oral secretions may be associated with failed NIV use including: delay</td>
</tr>
</table>

Cross-sectional			respiratory appointments
Other (specify)	**Cohort**		

Aim of study: To explore factors associated with failed NIV use
Data collection method: Unclear
Sample size: 157
Identification/recruitment: Recruited consecutively

Measures

Tolerance
Ambulatory status
Use of NIV

Details of technology/NIV

Not reported

in NIV initiation until pending appointments; use of CPAP or bilevel ventilators with spontaneous mode; unawareness of pending acute respiratory failure and need to use NIV, particularly in ambulatory and respiratory onset patients; use of morphine in successful NIV users because of hospice protocols; and if settings not adjusted as respiratory status changes.

Cazolli 2013/2017
Journal paper / <u>conference abstract</u>
Country: USA

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	**Cohort**

Aim of study: To develop and test an oral secretion scale
Data collection method: Data collected at clinic and home visits
Sample size: 135/159

Participant characteristics:

Type of group	Patients
Condition	ALS/MND
Onset	43% bulbar signs
Sex	
Age	
NIV usage	Better tolerated in 118 patients
Other (specify)	Pharmacological agents were used by 44%

Measures

Adherence
Tolerance
Effective use of Mechanical I-Exsufflation

Details of technology/NIV

Oral secretion scale categorises

Data relating to NIV provision and usage:
A higher score on the oral secretion scale at initiation of NIV is associated with improved adherence/tolerance of NIV. Suctioning cleared the airway but was ineffective in maintaining it. Use of medication to control saliva was more effective when patients scored between 2 and 4 on the scale.
2017 abstract - An OSS score of 4 was associated with better tolerance of NIV.A score of 1 reliably signals the inability to maintain upper airway clearance.
Author conclusions:
Use of the scale may be helpful in managing patients undergoing NIV

<table>
<tr>
<td>Identification/recruitment: Unclear</td>
<td>severity of secretions in relation to changes in swallowing and coughing. 4=normal saliva swallow, 0=severe drooling.</td>
<td>intervention.</td>
</tr>
<tr>
<td>Cederbaum 2001
<u>Journal paper</u> / conference abstract
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up: 9 months</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>
Aim of study: To describe the behaviour of physicians and criteria for initiating mechanical ventilation
Data collection method: Data collected during a trial
Sample size: 387
Identification/recruitment: Unclear</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>7% received BiPAP
35 patients used mechanical ventilation</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
FVC%
Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
More rapidly progressing patients were given mechanical ventilation
Baseline ALSFRS were similar for those given ventilation and those not.
Mean FVC% was about 50% for those on intermittent ventilation and 30% for those on continuous at the start.
Patients at some sites did not use mechanical ventilation, at other sites it was provided to 50% of study participants.

Author conclusions:
Patients began ventilation at a wide range of values of FVC%, centres differed in their practice. Factors affecting use are complex.</td>
</tr>
<tr>
<td>Chakrabarti 2011
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up: 12 months</td></tr>
</table></td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>9 male</td></tr>
<tr><td>Age</td><td>Mean 62</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures</td>
<td>Data relating to NIV provision and usage:
Mask leak did not correlate with minute volume or ventilator triggering
Falling minute ventilation was linked to worsening disability in MND patients receiving domiciliary NIV despite apparently adequate ventilation assessed by overnight oximetry</td>
</tr>
</table>

<table>
<tr>
<td>
<table>
<tr><td></td><td></td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>

Aim of study: To analyse patient-ventilator interaction
Data collection method: PVI was performed by interrogation of the Encore © Smartcard storage.
Sample size: 10
Identification/recruitment: Unclear
</td>
<td>
ALS-FRS score
Usage
Tidal volume
Oxygen saturation via pulse oximetry

Details of technology/NIV
Respironics © Synchrony 2 ventilator;
</td>
<td>
A marked decreases in ventilator triggering and minute ventilation did not necessarily translate into "suboptimal" oximetry

Author conclusions:
Oximetry is an insensitive measure, and analysis of patient-ventilator interaction may be an important adjunct to oximetry.
</td>
</tr>
<tr>
<td>
Chaudri 2000
<u>Journal paper</u> / conference abstract
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To evaluate the use of SNIP
Data collection method: Data collected at clinic
Sample size: 59
Identification/recruitment: Consecutive
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>31 bulbar, 28 non bulbar</td></tr>
<tr><td>Sex</td><td>More males in bulbar group</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Blood gas levels
Sniff nasal inspiratory pressure

Details of technology/NIV
SNIP measure taken with hand-held meter
</td>
<td>
Data relating to NIV provision and usage:
In patients with normal bulbar function SNIP is related to vital capacity, and thereby respiratory muscle function.

Author conclusions:
Bulbar patients had low results due to difficulty in sealing the mouth rather than more severe respiratory muscle involvement.
SNIP is a simple and easy alternative to vital capacity to measure respiratory muscle function. Patients attending clinic should have both measured. Patients with a value below 30% are at risk of developing hypercapnia and should have arterial blood gases measured.
</td>
</tr>
<tr>
<td>
Chechyk 2017
Journal paper / <u>conference abstract</u>
Country: Belarus
<table>
<tr><td>RCT</td><td></td></tr>
</table>
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
</table>
</td>
<td>
Data relating to NIV provision and usage:
Highest AHI index was in patients with bulbar form.
</td>
</tr>
</table>

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<table>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To investigate use of polysomnography to detect sleep disordered breathing
Data collection method: Unclear
Sample size: 61
Identification/recruitment: Not reported
</td>
<td>
<table>
<tr><td>Sex</td><td>32 female 29 male</td></tr>
<tr><td>Age</td><td>Median 62</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Oxygen saturation
Apnoea/hypnoea Index

Details of technology/NIV
Not reported
</td>
<td>
Author conclusions:
Polysomnography is an informative diagnostic method for choice of treatment and timely NIV.
</td>
</tr>
<tr>
<td>
Chio 2001
<u>Journal paper</u> / conference abstract
Country: Italy
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To gather information on management of patients across the neurology centres
Data collection method: Questionnaire
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Staff from neurological departments</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not applicable</td></tr>
<tr><td>Sex</td><td>N/A</td></tr>
<tr><td>Age</td><td>NA</td></tr>
<tr><td>NIV usage</td><td>N/A</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Survey responses

Details of technology/NIV
Not reported
</td>
<td>
Data relating to NIV provision and usage:
An integrated health team existed in all large centres but only 14% of smaller ones.
Respiratory management seemed lacking in both large and small centres, NIV proposed by only 70% of large and 50% of smaller centres. Patients underwent NIV more often in large centres (p=0.03).
Discussion of respiratory issues was often late in the course of the disease when symptoms appeared.
Follow up visits scheduled average 9.3 weeks in large centres and average 10.6 weeks in small centres.
Respiratory function was checked
</td>
</tr>
</table>

<table>
<tr>
<td>Sample size: 36 centres
Identification/recruitment:
Responders to survey</td>
<td></td>
<td>at every follow up visit in 7 large and 9 small centres, every other visit in 2 large and 2 small centres, and only when symptoms were present in 3 small centres.
Author conclusions:
Centres often discussed respiratory status late and the attitude towards NIV could be negative.</td>
</tr>
<tr>
<td>Chio 2006
<u>Journal paper</u> / conference abstract
Country: Italy
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Review of clinic data</td></tr>
</table>
Aim of study: To evaluate the effects of tertiary centres
Data collection method: Data from a register
Sample size: 97 + 124
Identification/recruitment: Identified from a register</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Frequency of NIV recommendation

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
Centres had interdisciplinary teams, patients seen around every 8 weeks.
NIV offered for respiratory symptoms when FVC was below 50% of that predicted or when nocturnal pulse oximetry showed marked desaturations.
Patients attending general neurology clinics underwent NIV less often than the tertiary centre (6.5 versus 15.4 p=0.04).
Author conclusions:
Tertiary ALS centres improve outcomes in patients with ALS possibly through better implementation of supportive treatments. The tertiary centres also succeeded in following up their patients mainly through clinic based visits.</td>
</tr>
<tr>
<td>Chio 2012
<u>Journal paper</u> / conference abstract
Country: Italy
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
</table>
</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
Young male patients and subjects attending the tertiary ALS centres were more likely to undergo NIV.
Increase in NIV use over the time</td>
</tr>
</table>

BA		**NIV usage**	
Comparator:		**Other (specify)**	
Length of follow up:			
Mixed method			
Cross-sectional			
Other (specify)	Routine data analysis		

Aim of study: To explore characteristics of NIV users
Data collection method: Data from a register
Sample size: 1260
Identification/recruitment: All on register

Measures

NIV use

Details of technology/NIV

Not reported

period was limited to patients attending tertiary centres

Author conclusions:
Sociocultural factors, such as age, gender and marital status, strongly influence the probability of undergoing NIV. Efforts should be made to remove these obstacles

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Chum 2016
Journal paper / <u>conference abstract</u>
Country: Australia

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	X
Other (specify)	

Aim of study: To find out practice patterns and knowledge regarding NIV
Data collection method: Survey
Sample size: 305
Identification/recruitment: Identified

Participant characteristics:

Type of group	Respiratory physicians
Condition	N/A
Onset	N/A
Sex	N/A
Age	N/A
NIV usage	N/A
Other (specify)	50% of respiratory physicians and 30% of neurologists who responded did not see MND patients.

Measures

Survey responses

Details of technology/NIV

Not reported

Data relating to NIV provision and usage:
The three main perceived barriers to NIV therapy were severity of bulbar impairment, cognitive impairment and social isolation.
The rate of NIV therapy use in MND patients by the respiratory physicians and neurologists was 75% and 29% respectively.
Author conclusions:
Rates of NIV use were high (75%) with 80% of patients reported to have been successfully established on NIV.

<table>
<tr><td>via professional organisation</td><td></td><td></td></tr>
<tr>
<td>
Cooper-Knock, 2011
<u>Journal paper</u> / conference abstract
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Case study</td></tr>
</table>
Aim of study: To report use of subcutaneous glycopyrrolate as a treatment for excess saliva
Data collection method: Descriptive
Sample size: 1
Identification/recruitment: Not reported
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>Bulbar</td></tr>
<tr><td>Sex</td><td>F</td></tr>
<tr><td>Age</td><td>51</td></tr>
<tr><td>NIV usage</td><td>Less than hour per night increased to 4-6 hours.</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table>
<tr><td>NIV usage</td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>N/A</td></tr>
</table>
</td>
<td>
Data relating to NIV provision and usage:
Sublingual atropine was only transiently effective. She did not tolerate hyoscine hydrobromide patches because of blurred vision. Oral amitriptyline and salivary gland botulinum toxin injections produced only slight improvement. Enteral propantheline improved her symptoms during the daytime, but failed to control the nocturnal sialorrhoea,
She was treated with an overnight subcutaneous infusion of 600 micrograms of glycopyrrolate over 12 hours via a syringe driver, which improved her symptoms and allowed her to use NIV for periods of 6 – 8 hours.
Author conclusions:
Glycopyrrolate appears to be more effective and better tolerated than alternatives for the management of secretions in ALS. Its usage enabled increased use of NIV.
</td>
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<tr>
<td>
Copsey, 2016
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
</table>
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table>
<tr><td>Referral</td></tr>
</table>
Details of technology/NIV
</td>
<td>
Data relating to NIV provision and usage:
A significantly greater proportion of patients were referred to the regional respiratory service in the post-care centre cohort for consideration of non-invasive ventilation (NIV) (74.3% vs. 63.5%, p=<0.05), although there was no significant difference in the proportion of referred patients offered the treatment.
</td>
</tr>
</table>

<table>
<tr>
<td>
<table>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Record review</td></tr>
</table>
Aim of study:
Data collection method: Examination of records
Sample size: 74 and 144
Identification/recruitment:
</td>
<td>Not reported</td>
<td>Author conclusions:
Consolidating the care of patients in a specialist environment increased the proportion of patients living with MND who were referred for NIV.</td>
</tr>
<tr>
<td>
Cousins, 2013/2011/2012
<u>Journal paper</u> / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To understand non-acceptance of NIV
Data collection method: Administration of questionnaires
Sample size: 27
Identification/recruitment: Part of wider study
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>18 limb onset, 9 bulbar onset</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
ALS-FRS
Dyspnoea Rating Scale
Epworth Sleepiness Scale
Carer Distress Scale
Resilience

Details of technology/NIV
Not reported
</td>
<td>
Data relating to NIV provision and usage:
There was no statistical difference between those with limb and those with bulbar onset in tolerance of NIV (p=0.58) There was also no difference in disease characteristics at time of being offered.
Caregiver resilience commitment differed between those who accepted and those who declined.
Author conclusions:
There was no differences in MND symptomatology between those patients who tolerated NIV and those that did not; similarly, there was no difference in caregiving distress, indicative of no difference in ‘job demands’. However, there was a strong caregiver influence between the two groups in terms of caregiver dispositional and coping style variables.
The key predictor of uptake of NIV treatment was caregiver commitment: resilience. Caregivers should be seen as critically important in NIV usage and there
</td>
</tr>
</table>

<table>
<tr>
<td></td>
<td></td>
<td>should be a supportive programme for family caregivers as part of the care package for MND.</td>
</tr>
<tr>
<td>Crescimanno 2015/2016/2014
<u>Journal paper</u> / <u>conference abstract</u>
Country: Italy
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To evaluate the effect of PEEP
Data collection method: Data from two consecutive nights use, PEEP one night.
Sample size: 17
Identification/recruitment: Not reported</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Average 64</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Polysomnographies ECG recording during sleep

Details of technology/NIV
Idea Ultra ResMed</td>
<td>Data relating to NIV provision and usage:
No significant differences in nocturnal gas exchanges were found. N3 sleep stage duration was significantly lower and Arousal/Awakening index was significantly higher with the PEEP setting 2 (p= 0.03 and p=0.04, respectively).

Author conclusions:
Background Expiratory positive pressure application did not result in advantage on nocturnal gas exchange and was associated with worse sleep quality, higher sleep fragmentation, and higher sympathetic activity in comparison to no PEEP.</td>
</tr>
<tr>
<td>Cuvelier 2010
Journal paper / <u>conference abstract</u>
Country: France
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
</table>
</td>
<td>Participant characteristics:
Measures
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>36 peripheral, 14 bulbar</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td>Half were initiated on NIV during an acute respiratory failure episode</td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
A vital capacity <25% pred. and/or a PImax and/or a sniff nasal-inspiratory pressure (SNIP) <=15 cmH2O were always associated with hypoventilation. Hypoventilation was never present when VC >50% pred. and when PImax and/or SNIP >50 cmH2O. Isolated elevated diurnal HCO3- occurred only when PImax and/or</td>
</tr>
</table>

<table>
<tr>
<td>
<table>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>
Aim of study: To identify data predicting hypoventilation
Data collection method: Collected at routine 3 monthly appointment
Sample size: 50
Identification/recruitment: Consecutive
</td>
<td>
Pulmonary function tests

Details of technology/NIV
Not reported
</td>
<td>
SNIP were between 50 and 30 cmH2O. Peak cough flow did not predict HV.

Author conclusions:
Routine clinical assessments of ALS patients at stable state do not require to include blood gas analysis until PImax and/or SNIP <=50 cmH2O.
Nocturnal tests for screening or early identification of HV (oxymetry, capnography) are at best indicated below this 50 cmH2O PImax/SNIP threshold value.
</td>
</tr>
<tr>
<td>
De Vito 2012
<u>Journal paper</u> / conference abstract
Country: Argentina
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Case studies</td></tr>
</table>
Aim of study: To report 3 case studies
Data collection method: Description
Sample size: 3
Identification/recruitment: Not reported
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>1 developed bulbar symptoms</td></tr>
<tr><td>Sex</td><td>2 female 1 male</td></tr>
<tr><td>Age</td><td>45, 51, 57</td></tr>
<tr><td>NIV usage</td><td>Continuous</td></tr>
<tr><td>Other (specify)</td><td>Non measurable VC</td></tr>
</table>
Measures
Descriptive

Details of technology/NIV
High span inspiratory positive airway pressure (16 to 20 cm H2O) and an expiratory positive airway pressure of 4 to 6 cm H2O, with a back-up rate of about 16 per minute.
</td>
<td>
Data relating to NIV provision and usage:
All patients refused tracheostomy. Patients survived for 16 months, 15 months and 27 months of full time full-setting NIV at home. For two patients their vital capacity was non-measurable for the last 5-7 months.
All patients' dyspnea and hypoventilation were completely relieved despite loss of all breathing ability (VC non-measurable) and they could only talk because of the pressure delivered by the BiPAP.
Key points for management were clinical vigilance, repeated measurement of vital capacity, coughing ability, cough assist with ambu bag, oxygen saturation overnight monitoring and advance planning.
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<td></td>
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<td>Author conclusions:
Full-setting continuous non-invasive ventilation is feasible at home, rather than resorting to tracheostomy even for patients with non-measurable vital capacity . Survival can be prolonged, wellness optimised and managed at home, and a peaceful death can be achieved.</td>
</tr>
<tr>
<td>Desai 2012/2011/2012
Journal paper / <u>conference abstract</u>
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
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<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To explore the use of home based sleep study
Data collection method: Studied over 3 months
Sample size: 15/26
Identification/recruitment: Consecutive</td>
<td>Participant characteristics:
Measures
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table></td>
<td>Data relating to NIV provision and usage:
ALS patients have difficulty tolerating multichannel polysomnography because of weakness, reduced mobility, secretions, dysarthria hampering communication, "first-night effect". Standard daily respiratory measures FVC and NIF minimize the degree of respiratory insufficiency present in ALS patients at first evaluation. Only 4 of the 15 patients qualified for NIV based on FVC less than 50% but of the remaining 11 patients, 7 had elevated AHI and 9 had elevated RDI which would have indicated NIV.
Author conclusions:
Home based unattended sleep study by peripheral arterial tonometry for early NIV indication should be an integral part of the initial ALS multidisciplinary clinic evaluation.</td>
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<table>
<tr>
<td></td>
<td>Peripheral arterial tonometry
Apnea Hypopnea Index
Polysomnography
Sitting and supine FVC
NIF(Negative Inspiratory Force)
sleep efficiency,
RDI(Respiratory Disturbance Index)
ODI(Oxygen Desaturation Index

Details of technology/NIV
Watch PAT100 (Itamar Medical)</td>
<td></td>
</tr>
<tr>
<td>Doddamreddy 2017
Journal paper / <u>conference abstract</u>
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
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<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Review of case notes</td></tr>
</table>
Aim of study: To investigate the optimal timing of NIV
Data collection method: Review of notes
Sample size: 96
Identification/recruitment: Patients seen at a referral centre</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>Respiratory 75%
bulbar 60%</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Mean 63</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
FVC
Time of initiation

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
Mean FVC at NIV initiation was 51.6%.
Early NIV (initiated at FVC>50) was implemented in 51% of patients due to respiratory (67%) or bulbar symptoms (52%)
NIV was implemented in 49% of patients per practice guidelines (FVC<=50).

Author conclusions:
Majority of patients were initiated on nocturnal NIV appropriately or earlier than current practice guidelines due to respiratory or bulbar symptoms.</td>
</tr>
<tr>
<td>Donvito 2017</td>
<td>Participant characteristics:</td>
<td>Data relating to NIV provision</td>
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Journal paper / <u>conference abstract</u>
Country: Italy
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<tr><td>RCT</td><td></td></tr>
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<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To explore the use of a digital amplifier
Data collection method: Questionnaires
Sample size: 5 patients
Identification/recruitment: Unclear
</td>
<td>
Measures
<table>
<tr><td>Communication Effectiveness Index-Modified Comprehensibility for caregivers rating</td></tr>
</table>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>No bulbar involvement</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>At least 16 hours per day</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>Transdermal amplifier on the larynx
NIV with oronasal mask</td></tr>
</table>
</td>
<td>
and usage:
Quality of communication perceived by patients improved with the amplifier (CETI-M score NA mean 18,2/70; CETI-M score A mean 42/70).
Partners' comprehension of speech was better combining NIV with the digital voice amplifier (CQ 1-score NA 1.8/A 3.4; CQ 2-score NA 3/A 2.2; CQ 3-score NA 2.8/A 2; CQ 4-score NA 5/A 1.8; CQ 5- score NA 2.4/A 1.6).

Author conclusions:
Use of a digital voice amplifier in ALS patients without bulbar involvement improves quality of communication between patients and their caregivers during NIV.
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<td>
Elman 2003
<u>Journal paper</u> / conference abstract
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
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<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
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<td>
Participant characteristics:
Measures
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td>None were using NIV</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>
Data relating to NIV provision and usage:
The average minimum oxygen saturation was 80.2% plus/ minus 8.8%(minimum, 49%; maximum, 92%).
The average mean oxygen saturation was 93.8% plus/minus 2.1% (minimum, 86%; maximum, 98.1%). The average percentage of time spent with oxygen saturation at less than 88% was 2.8% plus/minus 9.6% (maximum, 82.2%; minimum, 0%). The average number of desaturation events per hour was
</td>
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<table>
<tr>
<td>Aim of study: To determine the appropriateness of nocturnal nasal ventilation
Data collection method: Data collected in patient home.
Sample size: 78
Identification/recruitment: Consecutive</td>
<td>Total recording time
Time oxygen saturation below 88%
Oximeter measured the lowest saturation
eFVC or e%FVC

Details of technology/NIV
Respironics 920M</td>
<td>1.1 plus/ minus 0.9 (maximum, 3.6; minimum, 0).
While 24 patients were ineligible for NIV based on spirometry results, they displayed, on average, two desaturations per hour, a mean saturation of 93%, and a mean lowest percentage saturation of 79%.
Desaturations are indicative of hypoxemia during sleep that is suggestive of hypoventilation and inspiratory muscle weakness rather than simple sleep-disordered breathing with central or obstructive apneas
Author conclusions:
The recommendation that FVC be below 50% of normal is inappropriate for justifying introduction of nocturnal nasal ventilation. Many patients are symptomatic at higher FVC and have nocturnal hypoxemia. Nocturnal oximetry is a valuable tool for identifying nocturnal hypoxemia, and may identify a need for NIV sooner than FVC measurement guidelines.</td>
</tr>
<tr>
<td>Fantine 2016
<u>Journal paper</u> / conference abstract
Country: Italy
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
</table>
</td>
<td>Participant characteristics:
Measures
<table>
<tr><td>Type of group</td><td>Patients and healthy volunteers</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>30 male 11 female</td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
High correlation was found between all diaphragm thickness parameters and FVC and SNIP values.

Author conclusions:
Diaphragm thickness assessed by ultra-sound is feasible as an option for assessing initial ventilator failure</td>
</tr>
</table>

Length of follow up: **Mixed method** **Cross-sectional** X **Other (specify)** **Aim of study:** To explore the value of diaphragmatic thickness as a measure of lung function impairment **Data collection method:** Unclear **Sample size:** 41 patients **Identification/recruitment:** Patients attending a centre (details unclear)	Spirometry SNIP Diaphragm ultra sound evaluation Arterial blood gases **Details of technology/NIV** N/A	and significantly correlates with global respiratory alterations in patients with ALS.
Farrero 2005 **Journal paper / conference abstract** **Country: Italy** **RCT** **Non-RCT** **CBA** **BA** **Comparator:** **Length of follow up:** **Mixed method** **Cross-sectional** **Other (specify)** Case note review **Aim of study:** To analysis the impact of introducing a protocol for home ventilation **Data collection method:** Case note review **Sample size:** 86 **Identification/recruitment:** All at a tertiary care centre	**Participant characteristics:** **Type of group** Patients **Condition** ALS **Onset** 22 bulbar **Sex** **Age** **NIV usage** **Other (specify)** Measures Survival Details of technology/NIV Not reported	**Data relating to NIV provision and usage:** Prior to the protocol the majority of patients began treatment with HMV during an acute episode requiring ICU admission (p = 0.001) and tracheal ventilation (p = 0.025), with a lower percentage of patients beginning HMV treatment without respiratory insufficiency (p = 0.013). Multivariate analysis showed bulbar involvement to be an independent prognostic factor for survival (relative risk, 1.6; 95% confidence interval, 1.01 to 2.54; p = 0.04) No significant differences in survival were observed between patients with bulbar involvement following treatment with NIV and those with intolerance, except for the subgroup of patients who began NIV treatment with hypercapnia (p = 0.0002). **Author conclusions**: Further studies are required to

<table>
<tr>
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<td>confirm the benefits of NIV treatment in patients with bulbar involvement,</td>
</tr>
<tr>
<td>Garabelli 2013
Journal paper / conference abstract
Country: Italy
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr><tr><td>Other (specify)</td><td>Cohort</td></tr></table>
Aim of study: To describe the NIV pathway
Data collection method: Clinical tests
Sample size: 78
Identification/recruitment: Described as selecting patients in “a randomised way”</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>Not clear</td></tr><tr><td>Sex</td><td>Not reported</td></tr><tr><td>Age</td><td>Not reported</td></tr><tr><td>NIV usage</td><td>Not reported</td></tr><tr><td>Other (specify)</td><td></td></tr></table>
Measures
FVC

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:

Author conclusions:
EPAP set higher than 4 cm H2O to reduce ODI, normalises VT and increase SpO2 in NIV permits better tolerance and adherence in all patients including those with bulbar impairment.
With proper care bulbar patients can have good tolerance.</td>
</tr>
<tr>
<td>Georges 2016
Journal paper / conference abstract
Country: France
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr></table></td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td></td></tr><tr><td>Sex</td><td></td></tr><tr><td>Age</td><td></td></tr><tr><td>NIV usage</td><td></td></tr><tr><td>Other (specify)</td><td></td></tr></table>
Measures
Criteria for initiation</td>
<td>Data relating to NIV provision and usage:
At NIV initiation, 90% of patients were symptomatic. Median PaCO2 was 48 mmHg. The main criterion to initiate NIV was 'symptoms' followed by 'hypercapnia' in 42% and 34% of cases, respectively. NIV was initiated on functional parameters in only 5% of cases. Guidelines were followed in 81% of cases</td>
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<table>
<tr><td>Other (specify)</td><td>Review of data</td></tr>
</table>
Aim of study: To explore the effect of guidelines on practice
Data collection method: Routine data from a referral centre
Sample size: 624
Identification/recruitment: All eligible
</td>
<td>
Details of technology/NIV
<table>
<tr><td>Not reported</td></tr>
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<td>
Author conclusions:
The majority of patients are treated at the stage of symptomatic daytime hypoventilation, which suggests that NIV is initiated late in the course of ALS
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Georges 2016
<u>Journal paper</u> / conference abstract
Country: France
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up: 3 months</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>
Aim of study: To highlight the importance of obstructive events
Data collection method: routine clinical data
Sample size: 190
Identification/recruitment: All eligible
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>175</td></tr>
<tr><td>Sex</td><td>81 male</td></tr>
<tr><td>Age</td><td>Mean 64</td></tr>
<tr><td>NIV usage</td><td>179 tolerated for more than 4 hours per night</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table>
<tr><td>Symptoms (including NIV-related discomfort), Blood gases, Ventilator data Nocturnal oximetry nap polygraphy (or polysomnography)</td></tr>
</table>
</td>
<td>
Data relating to NIV provision and usage:
Among the 179 patients, after correction of leaks, 73 remained inadequately ventilated at night (defined as more than 5% of the night spent at <90% of SpO2), as a result of obstructive events in 67% of cases (n=48). Patients who remained inadequately ventilated after optimal adjustment of ventilator settings presented with shorter survival than adequately ventilated patients.
Patients with upper airway obstructive events without nocturnal desaturation and in whom no adjustment of treatment was therefore performed also presented with shorter survival.
Adjustments of ventilator settings can control obstructive events in 58% of cases, with no survival difference between patients corrected during treatment and those who were immediately adequately ventilated. The most frequently effective treatment was to try to reduce upper airway collapsibility by increasing EPAP to
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<td></td>
<td>Details of technology/NIV

NIV was initiated according to the current standardized procedure in the department, over a period of 3 to 5 days. Built-in monitoring software was used to detect air leaks, which were then corrected.

increased expiratory
positive airway pressure (EPAP) to the maximum of our protocol (10 cm H20) for 18 patients
Use of self-adapting inspiratory pressure devices in 8 patients
IVAPS mode,Resmed, Sydney, Australia or AutoAdvanced mode, Philips Respironics, Pensylvania,USA) for 3 patients,
3/ switch to volume-controlled mode in 1 patient (VT 500ml, Ti1,3 EPAP 4).
custom-made mandibular advancement device, was tried in addition to NIV in 4 patients, but was discontinued after 3 to 6 months due to poor tolerance.
The oronasal mask was replaced by a nasal mask, which was not supported by the patients concerned due to air leaks.
Anterior dislocation of the jaw using a cervical collar was tried, but without success, in 3 patients.</td>
<td>high levels. Unfortunately, this was not always effective.
Nocturnal SpO2 monitoring is probably not sufficiently precise to detect poor quality sleep in patients with obstructive events or the criteria of nocturnal SpO2 < 90% for more than 5% of the nocturnal recording time could be too high.
Author conclusions:
Upper airway obstruction during NIV occurs in patients with ALS and is associated with poorer prognosis. Such events should be identified as they can be corrected by adjusting ventilator settings. Upper airway obstruction is one of the mechanisms of NIV failure.</td>
</tr>
<tr>
<td>Gonzalez-Bermejo 2011
Journal paper / <u>conference abstract</u>
Country: France</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr></table></td>
<td>Data relating to NIV provision and usage:
The median survival from NIV onset was 15 < 4 months in the v-NIV</td>
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<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To compare pressure preset NIV to volume preset NIV
Data collection method: Compared data from 2 centres
Sample size: 62 + 82
Identification/recruitment: Not reported
</td>
<td>
Measures
Survival

Details of technology/NIV
Not reported
<table>
<tr><td>Onset</td><td>32 bulbar onset</td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td>Average 62</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>cohort, versus 17 +/- 4 months in the p-NIV cohort (p = 0.4).
PaCO2 under NIV was an independent prognostic factor (HR = 1.1, p = 0.009), irrespective of the ventilatory mode used.

Author conclusions:
The two settings provided similar survival. Adequate NIV (measured by PaCO2) is more important than the ventilator mode.</td>
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<td>
Gonzalez-Calzada
<u>Journal paper</u> / conference abstract
Country: Spain
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Case note review</td></tr>
</table>

Aim of study: To explore factors predicting survival
Data collection method: Routine data
</td>
<td>
Participant characteristics:
Measures
FVC
Survival

Details of technology/NIV
Not reported
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
The identified risk factors for mortality were severity of bulbar involvement (HR 2), Forced Vital Capacity (FVC) % (HR 0.99) and ALSFRS-R (HR 0.97).

Author conclusions:
A better assessment of bulbar involvement, including evaluation of the upper airway, and a careful titration on NIV are necessary to optimize treatment efficacy.</td>
</tr>
</table>

Sample size: 213
Identification/recruitment: All eligible

Gonzelez-Bermejo 2013
Journal paper / **conference abstract**
Country: France

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up: one year	
Mixed method	
Cross-sectional	
Other (specify)	Cohort

Aim of study: To investigate whether the quality of NIV effects impacts
Data collection method:
Sample size: 82
Identification/recruitment: Unclear

Participant characteristics:

Type of group	Patients
Condition	ALS
Onset	Bulbar patient numbers "low"
Sex	
Age	
NIV usage	Minimum 4 hours per night
Other (specify)	

Measures

Symptoms
Arterial blood gases
Nocturnal pulsed oxygen saturation – SpO_2

Details of technology/NIV

(VPAP-III or VPAP-IV, Resmed, Sydney, Australia) featuring automatic ventilatory signal analysis (Reslink ® , Resmed, Sydney, Australia)

Data relating to NIV provision and usage:
40 patients were considered correctly ventilated at month one.
Of those who were considered not to be correctly ventilated, corrective measures had been achieved in 12 patients by 6 months.
Inadequate ventilation in the first month was identified as a risk factor for mortality (p=0.029).
Leaks were identified as the main source of persistent nocturnal desaturations in 53% of cases. In 26% of cases, desaturations were related to ' obstructive events ', in 21% of instances neither leaks nor obstructive events were identified.
Every patient was ventilated in barometric, spontaneous-timed mode, with pressures adjusted in the clinic to patient comfort, leaks, and efficiency of ventilation.
Ventilator settings were titrated to relieve symptoms and, if possible, to achieve normal daytime PaO 2 , PaCO 2 , and SpO 2 . NIV was started with low inspiratory pressures (8 – 12 cm H 2 O) that were gradually titrated upward as tolerated by the patient.
Patients were instructed to use NIV for as long as tolerated at night and as necessary during the daytime.
All patients were also taught assisted cough techniques by an experienced respiratory

<table>
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<td></td>
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<td>physiotherapist.
NIV was considered adequately effective if symptoms and blood gases improved, no NIV-related dis-comfort was reported, and if nocturnal oximetry showed a time with an SpO 2 below 90% less than 5% of the time.
Corrective measures encompassed- optimization of mask fitting in the presence of excessive leaks; increase in expiratory positive airway pressure in the presence of obstructive events; increase in inspiratory positive airway pressure in the presence of persistent hypoventilation.
Author conclusions:
NIV did not adequately correct nocturnal desaturations in approximately half of patients. The more desaturations there are at the time of NIV initiation, the more difficult it is to achieve a satisfactory NIV.
An early assessment of NIV efficiency is important in ALS patients. Nocturnal pulse oximetry should be performed first.</td>
</tr>
<tr>
<td>Gruis 2005
<u>Journal paper</u> / conference abstract
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
</table>
</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>63& limb onset</td></tr>
<tr><td>Sex</td><td>48% female</td></tr>
<tr><td>Age</td><td>Mean 62</td></tr>
<tr><td>NIV usage</td><td>70% achieved more than 4 hours nightly</td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
72% were tolerant and 28% were not. Patients who were tolerant were more likely to have limb-onset symptoms and have higher FVCs at NIV initiation.
Patients initially contacted after one week then seen every 3 months.
NIV not started until secretions fully</td>
</tr>
</table>

Length of follow up: 4 years (until death) **Mixed method** **Cross-sectional** **Other (specify)** **Cohort** **Aim of study:** To identify predictors of tolerance **Data collection method:** **Sample size:** 139 (data only for 50) **Identification/recruitment:** Patients attending a clinic	**Other (specify)** Mean FVC at start 46.7 Measures Tolerance Details of technology/NIV	controlled. For sialorrhea, glycopyrrolate or transdermal hyoscine or, if pseudobulbar symptoms were present, amitriptyline was used. If patients failed or had a contraindication to pharmacologic treatment, they received botulinum toxin injections. Pressures were begun at 8 cm H2O inspiratory positive airway pressure and 3 cms H2O expiratory positive airway pressure using heated humidification and NasalAire interfaces to minimize nasal congestion and claustrophobia from large masks. If nasal congestion continued intranasal steroid sprays were prescribed. The inspiratory positive airway pressure was increased by 2 cm H2O increments weekly until symptoms improved if respiratory symptoms continued. **Author conclusions**: Duration of disease and age were not predictors of tolerance, limb onset was the most important predictor.
Gruis 2006 **Journal paper / conference abstract** **Country: USA** **RCT** **Non-RCT** **CBA** **BA** **Comparator:**	**Participant characteristics:** **Type of group** Patients **Condition** ALS **Onset** 36 limb onset **Sex** 32 male **Age** Average 61 **NIV usage** **Other (specify)** Median FVC at	**Data relating to NIV provision and usage:** 18 were tolerant of NIV and 19 were intolerant All patients were started on nocturnal NIPPVat 8 and 3 cm H2O inspiratory and expiratory pressure, respectively. Nasal-Aire interfaces were initially

Length of follow up:			
Mixed method			
Cross-sectional			
Other (specify)	**Cohort**		

Aim of study: To explore pressure settings in NIV
Data collection method:
Sample size: 36
Identification/recruitment: Identified by chart review

	initiation 48.5 Suction prescribed for 21

Measures

Survival

Details of technology/NIV

Three titrated by polysomnogram because of more prominent nocturnal symptoms

tried. If patients could not tolerate this, they were fitted with a traditional mask. Alternative masks were tried if discomfort was experienced. Heated humidification was used to minimize nasal congestion and nasal steroids were prescribed if this was insufficient. Patients were contacted after 1–2 weeks by telephone to determine whether respiratory symptoms had improved. Follow up visits occurred every 3 months.
Once symptoms developed, or if symptoms persisted despite initiation of NIPPV, the IPAP was increased by 2 cm H2O increments weekly until symptoms improved. If patients found the higher pressure settings to be intolerable or without symptomatic benefit, then the IPAP was returned to the previous setting and 1 cm H2O upward increments were attempted.
The maximum pressure needed for comfort by any patient in this study was 19/5 cm H2O, while 4 (22%) found the original 8/3 cm H2O settings to be sufficient until death. Tolerance to comfort and relatively low NIPPV inspiratory pressures is associated with improved survival.
Author conclusions:
ALS patients who are tolerant to NIPPV typically need at least one upward change in pressure settings. 78% had at least one change, 33% had at least two and 11% had at least three and 6% had

<table>
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<td>at least 4. The median time to the first change was 5 months; second change, 8 months; and third change, 22 months.</td>
</tr>
<tr>
<td>Hannan 2015
<u>Journal paper</u> / conference abstract
Country: Australia
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr><tr><td>Other (specify)</td><td>Case study</td></tr></table>Aim of study: To report a case study
Data collection method: Descriptive
Sample size:1
Identification/recruitment: Not reported</td>
<td>Participant characteristics:<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>Not reported</td></tr><tr><td>Sex</td><td>Male</td></tr><tr><td>Age</td><td>51</td></tr><tr><td>NIV usage</td><td>Not reported</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
Episodes of asynchrony /rapid cycling

Details of technology/NIV
Full face mask, ResMed VPAP IV ST in spontaneous/timed mode with inspiratory pressure 11cm H2O, expiratory pressure 5cm H20 and respiratory rate 12 breaths per minute. Trigger and cycle sensitivity were set to medium.</td>
<td>Data relating to NIV provision and usage:
Increasing the minimum inspiratory time to 1.2 seconds was effective in supressing episodes of asynchrony/autocycling.
When this is observed practice is to ensure that mask and tubing are free from condensation and that leak is minimised and that appropriate trigger and cycle sensitivity is set.
Author conclusions:
If other changes are not achieving improvement increasing the minimum inspiratory time should be trialled.</td>
</tr>
<tr>
<td>Heiman-Patterson 2017/2018
<u>Journal paper / conference abstract</u>
Country: USA
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr></table></td>
<td>Participant characteristics:<table><tr><td>Type of group</td><td>Specialists</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>N/A</td></tr><tr><td>Sex</td><td>N/A</td></tr><tr><td>Age</td><td>N/A</td></tr><tr><td>NIV usage</td><td>N/A</td></tr></table></td>
<td>Data relating to NIV provision and usage:
When considering NIV, US and EU specialists value upright FVC most but differ regarding upright MIP (US: 2nd; EU: 5th) and overnight pulse oximetry (US: 6th; EU: 2nd).</td>
</tr>
</table>

Comparator: **Length of follow up:** **Mixed method** **Cross-sectional** X **Other (specify)** **Aim of study:** To explore practice in initiation of NIV **Data collection method:** Survey **Sample size:** **Identification/recruitment:** Identified through professional organisations	**Other (specify)** **Measures** Current practice Details of technology/NIV Not reported	In patients without respiratory symptoms, most US specialists initiate NIV at FVC/SVC <50% predicted upright VC (US: 41/60 [68.3%]; EU: 10/39 [25.6%];p<.001); no single criterion was identified by most EU physicians. European respondents use overnight pulse oximetry (69.8% vs 7.9%; p<0.001) and arterial blood gas analyses (62.8% vs 3.2%; p<0.001) more than US respondents. US specialists more often refer patients to home agencies and trials/instructions occur at home (US: 39/57 [68.4%]; EU: 5/39 [12.8%];p<.001); EU specialists more often admit patients to hospital (US: 0/57 [0%]; EU: 16/39 [41.0%];p<.001). US specialists prefer to use certain ventilators non-invasively (US: 25/57 [43.9%]; EU: 5/39 [12.8%];p=.002); most EU specialists allow pulmonologists to decide (US: 11/57 [19.3%]; EU: 25/39 [64.1%];p<.001). Without influences of insurance/financial constraints, a greater number of US than EU specialists (US: 44/57 [77.2%]; EU: 6/39 [15.4%];p<.001) would alter when they prescribe NIV. **Author conclusions**: NIV prescribing differs between the

<table>
<tr><td></td><td></td><td>US and EU and may be influenced by insurance/financial constraints.</td></tr>
<tr><td>Howard 2010
Journal paper / <u>conference abstract</u>
Country: Australia
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up: Unclear</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td>X</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Aim of study: To evaluate an ambulatory model of NIV initiation before and after introduction of the new model
Data collection method: Audit
Sample size: Unclear
Identification/recruitment: All patients referred during time period</td><td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>Not reported</td></tr><tr><td>Sex</td><td>Not reported</td></tr><tr><td>Age</td><td>Not reported</td></tr><tr><td>NIV usage</td><td>Not reported</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
Time and deaths on the waiting list
Length of stay,
Adverse events and Polysomnography data

Details of technology/NIV
(VPAP III, Resmed, Sydney).</td><td>Data relating to NIV provision and usage:
The ambulatory model included a 3-hour stay to commence ventilation and receive education. This included mask fitting and adjustment of the spontaneous-timed mode bi-level pressure ventilator. Ventilator settings and education were finalised the following morning, with subsequent outpatient review.
The average waiting time to commence ventilation fell from 47.5 days to 9.9 days ($p < 0.01$) and the hospital length of stay fell from 4.3 to 2.0 days ($p = 0.06$) after changing to the ambulatory model. There were more adverse events on the waiting list prior to the model change (4 of 14 (3 deaths, 1 acute admission) pre vs 0 of 12 post, $p = 0.04$). There was no difference in polysomnographic indices of sleep quality or ventilation after changing to the new model.
Author conclusions:
Changing NIV implementation in MND to an ambulatory model reduced waiting time to commence ventilation, adverse events on the waiting list and hospital length of stay, with no change in the effectiveness of ventilation.</td></tr>
<tr><td>Inyat 2016
Journal paper / <u>conference abstract</u>
Country: UK</td><td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr></table></td><td>Data relating to NIV provision and usage:
Respiratory tract infections, mucus</td></tr>
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<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>
Aim of study: To evaluate a care pathway
Data collection method: Unclear
Sample size: Unclear
Identification/recruitment: Unclear
</td>
<td>
Measures
Management

Details of technology/NIV
Not reported
<table>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>
plugging, and secretion management difficulties were successfully identified by analysing tidal volumes and compliance data to allow intervention and prevent hospitalisation.

Author conclusions:
An integrated ventilation clinic and pathway facilitates accurate, comprehensive and tailored assessment, with precise real time monitoring of patients requiring domiciliary ventilation.
</td>
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<td>
Jackson 2001
<u>Journal paper</u> / conference abstract
Country: USA
<table>
<tr><td>RCT</td><td>X</td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator: Patients with oxygen desaturation below 90% based on nocturnal oximetry versus patients with FVC below 50% (standard care)</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To compare measures
</td>
<td>
Participant characteristics:
Measures
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>
Data relating to NIV provision and usage:
There was no significant correlation between FVC% and the ALSFRS-R, symptom score, MEP, MIP, or duration of nocturnal desaturation <90%.

Author conclusions:
FVC% correlates poorly with respiratory symptoms and suggests that MIP and nocturnal oximetry may be more sensitive measures of early respiratory insufficiency. Intervention with NIV earlier than current standard of care may result in improved quality of life
</td>
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</table>

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<tr>
<td>of need
Data collection method: Pulmonary tests
Sample size: 20
Identification/recruitment: Unclear</td>
<td>ALS functional rating scale-respiratory version (ALSFRS-R)
Pulmonary symptom scale,
Short form 36 (SF-36),
FVC%,
Maximal inspiratory pressure (MIP),
Maximal expiratory pressure (MEP),
Nocturnal oximetry.

Details of technology/NIV
Not reported</td>
<td></td>
</tr>
<tr>
<td>Jackson 2006
<u>Journal paper</u> / conference abstract
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Chart review</td></tr>
</table>
Aim of study: Examine factors associated with usage
Data collection method: Patients on a database
Sample size:403
Identification/recruitment: Not applicable</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Factors associated with use

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
NIV compliance was strongly correlated with symptoms of dyspnea and orthopnea as well as with the use of other therapies including PEG tubes, augmentative speech devices, and riluzole. Male gender and household income >$80,000 were also associated with higher NIV use.
There was no correlation between age, race, type of insurance, forced vital capacity, duration of symptoms, ALSFRS-R, caregiver burden or quality of life with the use of NIV.

Author conclusions:
These data suggest that the factors which are most closely associated</td>
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<tr>
<td></td>
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<td>with NPPV utilization are symptomatic orthopnea and dyspnea</td>
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<td>
Jackson, 2016/2009
Journal paper / <u>conference abstract</u>
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td>X Unclear process</td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator: Patients with FVC between 75-85% (early) versus patients with FVC 45-55% (usual care)</td></tr>
<tr><td colspan="2">Length of follow up: 12 months</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To evaluate the timing of intervention
Data collection method: Downloaded machine data, patient report questionnaires
Sample size: 57
Identification/recruitment: Unclear
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Compliance

Details of technology/NIV
Not reported
</td>
<td>
Data relating to NIV provision and usage:
Patients were educated about NIPPV prior to initiation.
Respiratory therapist visits were made three times the first week, twice the second and once in the third and fourth weeks with monthly visits during the rest of the study.
By week 4 after initiation of NIPPV, the compliance rate was 53.3% for Group 1 and 70.6% for Group 2. In Group 1, compliance steadily increased after 84 days on NIPPV so that after 364 days, there was 80% compliance. In Group 2, compliance was higher at all times and remained greater than 70% after 140 days.
In those subjects who were noncompliant at 28 days, 69.2% (9/13) remained noncompliant until death while 15.4% eventually became compliant; 15.4% became compliant only at terminal stages of disease.
For the non-compliant patients in both groups, the most frequent symptoms included: excessive dryness of the nose or throat passages (mean score 3.67), mask discomfort (3.28), air leakage from the mask (3.11), waking up frequently during the night (2.78), a sense of suffocation or claustrophobia (2.39), and soreness
</td>
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</table>

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<td>in the nose or throat passages (1.78). The remainder of symptoms did not appear to be related to non-compliance: running nose, headaches, ear pain, marks or rash on face, complaints from partner about noise from the machine, or bloating.
Author conclusions:
For both groups, initial compliance was maintained over the course of the study while those subjects who were non-complaint tended to remain so over the course of follow-up. There was an overall increase in compliance over time in both groups.
The majority of symptoms reported by patients within the first 4 weeks of initiating NIPPV are related to issues that are potentially resolvable with aggressive respiratory therapy intervention. Ensuring proper humidification and finding an interface that is comfortable and seals properly are imperative to improving compliance. This data supports the ability of asymptomatic patients to comply with NIPPV earlier in the course of the disease</td>
</tr>
<tr>
<td>Jacobs 2016
Journal paper / <u>conference abstract</u>
Country: USA
<table>
<tr><td>RCT</td><td>X</td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
</table>
</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
No difference was identified in weekly hours of use between IPAP and Bi-level PAP (linear repeated measure model; p=0.75).
Of the 16 subjects who provided preference data at study</td>
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<tr>
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<table>
<tr><td colspan="2">Comparator: BiPAP versus IPAP</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To compare inspiratory only positive airway pressure to bi-level positive airway pressure
Data collection method: Machine data
Sample size: 28
Identification/recruitment: Unclear
</td>
<td>
<table>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table>
<tr><td>Usage
Reported preference</td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>Not reported</td></tr>
</table>
</td>
<td>conclusion, 12 (75%) definitely or probably preferred IPAP to bi-level PAP.

Author conclusions:
IPAP was not associated with increased use over bi-level PAP but was preferred by patients.</td>
</tr>
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<td>
Jenkins 2014
Journal paper / <u>conference abstract</u>
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To investigate the effect of bulbar dysfunction on phrenic nerve studies
Data collection method: Test scores
Sample size: 100
Identification/recruitment: Not
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>69 spinal onset</td></tr>
<tr><td>Sex</td><td>41 female</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
</td>
<td>Data relating to NIV provision and usage:
We found a marked decline in the performance of all standard respiratory measures as a result of bulbar dysfunction alone.

Author conclusions:
Standard pulmonary function tests are of limited utility in the assessment of diaphragm dysfunction. The presence of modest bulbar disease leads to results so abnormal that the clinician is essentially blind to the true state of the diaphragm,</td>
</tr>
</table>

<table>
<tr>
<td>reported</td>
<td>Phrenic nerve conduction studies,
Upright and supine FVC,
Maximum inspiratory pressure (MIP),
Sniff nasal inspiratory pressure (SNIP),
ALSFRS- R and bulbar subscore

Details of technology/NIV
Not reported</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Johnson 2009
Journal paper / <u>conference abstract</u>
Country: UK
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr><tr><td>Other (specify)</td><td>Case note review</td></tr></table>
Aim of study: To explore outcomes from a service using home initiation of NIV
Data collection method: Case notes
Sample size: 42
Identification/recruitment: All patients in service</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>Not reported</td></tr><tr><td>Sex</td><td>Not reported</td></tr><tr><td>Age</td><td>Not reported</td></tr><tr><td>NIV usage</td><td>Not reported</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
Mean length of survival

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
Over 90% of patients with MND within the service have NIV initiated at home. This avoids hospital admission for initiation of NIV.
Our data indicate that it is safe and effective as mean length of survival is comparable to published data and patients prefer to have NIV initiated at home rather than in hospital. The level of patient satisfaction with the service is also very high.
The key factor in success is the ability to monitor symptoms and detect the early onset of ventilatory failure in an MDT setting, using equipment such as transcutaneous monitoring of CO2. The MND MDT is trained to recognize the early symptoms of respiratory failure. Early detection of symptoms is followed up by a team of specialist</td>
</tr>
</table>

<table>
<tr>
<td></td>
<td></td>
<td>nursing staff with expertise in respiratory management.
The respiratory team monitors patients regularly to optimize ventilatory settings and encourage early use of adjunctive therapies. This may include mechanical cough assistance and early antibiotic therapy.
Author conclusions:
Home initiation of NIV is safe and effective in MND.</td>
</tr>
<tr>
<td>Juntas-Morales, 2015
Journal paper / <u>conference abstract</u>
Country: France
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up: 18 months</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr><tr><td>Other (specify)</td><td>Cohort</td></tr></table>Aim of study: To investigate the role of clinical and functional parameters on NIV decisions and prognosis
Data collection method: Clinical data collected
Sample size: 135
Identification/recruitment: Unclear</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>Not reported</td></tr><tr><td>Sex</td><td>88 male, 47 female</td></tr><tr><td>Age</td><td>Not reported</td></tr><tr><td>NIV usage</td><td>Not reported</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
ALSFRS; SVC; FVC; and weight

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
The delay for starting NIV strongly correlated with ALS duration (R2=0.69, p<0.0001).
Delay for starting NIV is predictive of a bad prognosis of ALS and this is the stronger correlation found in this study

Author conclusions:
Respiratory function has to be monitored during the day and during the night at every stage of the disease as early changes may help physicians to better inform the patients about the potential progression of their disease. Studies should focus on demonstrating that NIV should be started earlier in the disease process.</td>
</tr>
<tr>
<td>Kareus 2006/2008
<u>Journal paper / conference abstract</u></td>
<td>Participant characteristics:</td>
<td>Data relating to NIV provision and usage:</td>
</tr>
</table>

Country: USA

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	X
Other (specify)	

Aim of study: To explore the value of adding a respiratory therapist to a MDT
Data collection method: Compared a group before to a different group after
Sample size: 37
Identification/recruitment: unclear

Measures

Useage
Survival

Type of group	Patients
Condition	ALS
Onset	
Sex	
Age	
NIV usage	
Other (specify)	

Details of technology/NIV

Not reported

Patients undergoing respiratory therapy were more likely to try non-invasive ventilation (odds ratio 4.01; 95% confidence interval 1.42-11.35) and more likely to use it for at least four hours per night (odds ratio 9.5, 95% confidence interval 2.32-38.88).

Author conclusions:
Adding a respiratory therapist to a multidisciplinary ALS clinic leads to an increase in the percentage of patients willing to try BiNIV as well as to use it more than four hours per night, and such use leads to prolonged survival.

Kartas 2011
Journal paper / conference abstract
Country: France

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Analysis of database

Aim of study: To explore how practice compares to recommendations

Participant characteristics:

Measures

Symptoms
Respiratory impairment

Type of group	Patients
Condition	ALS
Onset	Not reported
Sex	Not reported
Age	Not reported
NIV usage	Not reported
Other (specify)	

Details of technology/NIV

Not reported

Data relating to NIV provision and usage:
Symptoms were the main reason for NIV initiation (39%; only reason in 6 cases), followed by hypercapnea (28%).Functional respiratory impairment rarely came first (Pimax or SNIP in 3%; VC in 2%; nocturnal desaturation 3%).10% were ventilated due to acute respiratory insufficiency. At the time of NIV initiation, ninety percent of the patients reported symptoms (effort dyspnoea, dyspnoea at rest, orthopnoea, nocturnal arousals, daytime somnolence or morning headaches).

<table>
<tr>
<td>Data collection method: Data from a register
Sample size: 594
Identification/recruitment: All eligible patients in database</td>
<td></td>
<td>Sixtyfive patients (11%) were ventilated without demonstrating any of the consensus criteria for starting NIV.
Author conclusions:
At the time of starting NIV patients were very symptomatic and often hypercapnic, and had functional characteristics suggesting that NIV would have been started earlier if guidelines had been applied rigorously. There is insufficient resource allocation to the respiratory management of ALS,</td>
</tr>
<tr>
<td>Karwa 2015
Journal paper / <u>conference abstract</u>
Country: Unclear
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up: 2 years</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr><tr><td>Other (specify)</td><td>Cohort</td></tr></table>
Aim of study: To investigate diaphragm thickening as an indicator of respiratory muscle weakness
Data collection method: Ultrasound
Sample size: 4
Identification/recruitment: Unclear</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>Not reported</td></tr><tr><td>Sex</td><td>Not reported</td></tr><tr><td>Age</td><td>Not reported</td></tr><tr><td>NIV usage</td><td>Not reported</td></tr><tr><td>Other (specify)</td><td></td></tr></table>
Measures
Pulmonary function tests
ALS-FRS

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
Diaphragm ultrasound may pick up early changes in diaphragm such as asymmetry in muscle thickness between right and left and temporal decline in thickness. In addition this may be a useful tool in assess changes in muscle contractility.

Author conclusions:
Diaphragmatic ultrasound is a useful non-invasive method of evaluating respiratory function in patients with ALS, but the relevance of this tool in clinical practice is unclear.</td>
</tr>
<tr>
<td>Katz 2015
Journal paper / <u>conference abstract</u>
Country: USA</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr></table></td>
<td>Data relating to NIV provision and usage:
All patients adhered to NIV therapy,</td>
</tr>
</table>

<table>
<tr>
<td>
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To compare different NIV modes
Data collection method: Unclear
Sample size: 12
Identification/recruitment:
</td>
<td>
Measures
Adherence
Sleep quality,
Dyspnea,
Orthopnea,
Quality of life
Usage

<table>
<tr><td>Onset</td><td>No bulbar involvement</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Average 7.12 hours</td></tr>
<tr><td>Other (specify)</td><td>FVC < 65% of predicted and patient-reported dyspnea and orthopnea</td></tr>
</table>

Details of technology/NIV
Volume-targeted versus pressure-limited modes
</td>
<td>independent of treatment modality.
The second intervention period was associated with increased hours of use, independent of treatment mode.
The increased adherence in the second treatment period could suggest increased need as the disease progresses or that learning plays a role in adherence.

Author conclusions:
There was no statistically significant difference between the two modes of therapy for any measure.</td>
</tr>
<tr>
<td>
Ketterman 2016
Journal paper / <u>conference abstract</u>
Country: Germany
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
</table>
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients and carers</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Views and perceptions
</td>
<td>Data relating to NIV provision and usage:
ALS patients showed lower satisfaction with LTV (VAS 3.6/10, n=5) as compared to their relatives (VAS 6.6; n=14).
Patients evaluate LTV less positively than their relatives.
Decision-making of WLTV is a process of several months. In general, patients experience their decision of WLTVas an emotional relief. Family members supported</td>
</tr>
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Other (specify)	

Aim of study: To explore the emotional impact of the withdrawal of long term ventilation
Data collection method: Survey
Sample size: 8 patients, 20 relatives/care givers
Identification/recruitment: Identified before received ventilation
</td>
<td>
Details of technology/NIV

Not reported, unclear what type of long term ventilation
</td>
<td>
the patient decision of WLTV. In contrast, patients experience the attitude of professional care providers as less supportive
Latency between decision-making and realization of WLTV was 5.3 months. Patients informed their families about the decision of WLTV at different times:>12 month (n=4), >3 month (n=8); >1 month (n=4);<1 week (n=2). The patient's wish for WLTV was related to loss of communication (66%), followed by loss of mobility (44%) and hopelessness for cure (32%). The patient's option to determine his or her date of death by means of WLTV was experienced as a relief rather than a burden by all patients (10/10; n=6). However, emotions of family members were dominated by sadness (8.6/10) and the loss of a loved-one (8.3/10). Wishes of patients were more strongly backed by relatives (VSA 8.9/10) than by care providers (5.4/10)
Author conclusions:
There are different attitudes towards long term ventilation among patients, relatives and professional care givers.
</td>
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<td>

Kewin 2011
Journal paper / conference abstract
Country: UK

RCT	
Non-RCT	
CBA	
BA	
</td>
<td>

Participant characteristics:

Type of group	Patients
Condition	ALS
Onset	Not reported
Sex	Not reported
Age	Not reported
NIV usage	Not reported
</td>
<td>

Data relating to NIV provision and usage:
NIV was commenced within 2 weeks of assessment, although half were commenced within 48 hours
Those accepting NIV had a similar degree of respiratory failure to those that did not, but lived longer
</td>
</tr>
</table>

Comparator: **Length of follow up:** **Mixed method** **Cross-sectional** **Other (specify)** **Cohort** **Aim of study:** To evaluate current practice **Data collection method:** Unclear **Sample size:** 38 **Identification/recruitment:** All those referred	**Other (specify)** **Measures** Time to assessment Survival Details of technology/NIV Not reported	(210 versus 33 days) with good NIV compliance. **Author conclusions**: Early referral and assessment avoids crisis driven decision making, but the majority of patients were in respiratory failure requiring prompt intervention. Early specialist referral must be encouraged.
Khaliq 2009 **Journal paper** / **conference abstract** **Country:** UK **RCT** **Non-RCT** **CBA** **BA** **Comparator:** **Length of follow up:** **Mixed method** **Cross-sectional** X **Other (specify)** **Aim of study:** To evaluate use of a facemask to measure FVC and compare with spirometry in those with bulbar symptoms **Data collection method:** **Sample size:** 27 **Identification/recruitment:** Not	**Participant characteristics:** **Type of group** Patients **Condition** ALS **Onset** All with bulbar symptoms **Sex** 13 male **Age** Mean 64 **NIV usage** 11 were using NIV **Other (specify)** **Measures** FVC Spirometry Details of technology/NIV Not reported	**Data relating to NIV provision and usage:** All managed with a facemask, 14 failed to record anything with a mouthpiece. When FVC was recorded with both methods, FVC was greater using the facemask in all but one person, mean difference 0.65 litre (SD 0.43) $p<0.001$. **Author conclusions**: Facemask spirometry was acceptable to patients and none failed to record results, while 52% could not produce any result with a mouthpiece. The mean difference between the measures when both were available was clinically significant and could affect decision making regarding NIV

<table>
<tr><td>reported</td><td></td><td></td></tr>
<tr>
<td>
Khamanker 2018
<u>Journal paper</u> / conference abstract
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Examination of data</td></tr>
</table>
Aim of study: To explore the optimum point for NIV initiation
Data collection method: Examination of existing medical record data
Sample size: 474
Identification/recruitment: All meeting criteria
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Bulbar 27%, limb 69%</td></tr>
<tr><td>Sex</td><td>59% male</td></tr>
<tr><td>Age</td><td>38% over 65</td></tr>
<tr><td>NIV usage</td><td>403 users, 30% more than 8 hours per day</td></tr>
<tr><td>Other (specify)</td><td>38% used NIV + Cough Assist</td></tr>
</table>
Measures
<table>
<tr><td>Survival
Usage
ALSFRS-R percent predicted FVC</td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>No distinction was made on Bi-PaP brand or type</td></tr>
</table>
</td>
<td>
Data relating to NIV provision and usage:
The “optimized” NIV protocol (Bi-PAP initiation while FVC %predict ≥80, Bi-PAP usage >8 h/day, daily cough assist usage) has a 30. 8 month survival median, which is double that of a “standard” NIV protocol (initiation FVC %predict <50, usage >4 h/day, no cough assist).
Those at or above the 50 %predict threshold (N = 202, median = 24.10 months) at the time of Bi-PAP initiation,had a significant 18.7% associative increase in survival duration ($p < 0.01$).
Increasing the FVC %predict threshold to ≥ 60 (N = 250, median = 24.10 months) resulted in a significant 18.7% increase in survival duration compared to the standard < 50 FVC %predict threshold ($p < 0.001$).
The ≥ 70 FVC %predict group was nearly identical to the ≥ 60 group.
The ≥ 80 %predict Bi-PAP initiation group (N = 44) had a significant 25% associative increase in survival duration ($p < 0.01$) over the standard < 50 FVC %predict threshold group.
Those with FVC %predict ≥90 at Bi-PAP initiation (N = 23) lived 36.5% longer ($p < 0.01$) than users in the standard threshold (FVC %predict < 50) group.
Maximal associative survival benefit
</td>
</tr>
</table>

<table>
<tr>
<td></td>
<td></td>
<td>requires > 8 h/day of Bi-PAP usage. There was a significant difference (p < < 0.001) between Bi-PAP users who also used cough assist [median = 25.73 months] compared to Bi-PAP users who did not use cough assist. However, the gains of using Bi-PAP and cough assist in combination were not nearly as pronounced in the bulbar onset group as the limb onset group. Neither time since true onset nor baseline onset is a good predictor of when Bi-PAP should be started or a predictor of its overall associative survival benefit.
Author conclusions:
Time elapsed since ALS onset is not a good predictor of when NIV should be initiated. Earlier access to Bi-PAP and cough assist, prior to precipitous decline, is needed. The FVC %predict threshold value for Bi-PAP treatment initiation should be no less than 80%. Even bulbar patients, where NIV has been more controversial, had significant increases in survival.</td>
</tr>
<tr>
<td>Kim 2009/2010/2011
Journal paper / <u>conference abstract</u>
Country: South Korea
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
</table>
</td>
<td>Participant characteristics:
Measures
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td>Respiratory symptoms or signs</td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
The values of NC correlated well with the degree of nocturnal respiratory symptoms of the patients (r = -0.502 ~ -0.572, p = 0.003 ~ 0.011) and the compliance to the NIV treatments (r = 0.614 ~ 0.713, p= 0.000 ~ 0.004). However, the values of nocturnal hypoxia had no correlation with nocturnal</td>
</tr>
</table>

Mixed method		Compliance FVC ALS--FRS	symptoms of patients and only marginally correlated with compliance to NIV treatment. The degree of nocturnal hypercapnea correlated well with degree of respiratory distress during sleep (scores to 'orthopnea' questionnaire in ALSFRSr; r = -0.627 ~ - 0.491, P = 0.004 ~0.033) and compliance to NIV treatments (r = 0.539 ~0.649, P = 0.001 ~0.012). However the degree of nocturnal hypoxia, measured as duration of nocturnal hypoxia (defined as % of sleep when SaO2 < 95% per total sleep), average nocturnal SaO2, and minimal nocturnal SaO2 had no significant correlation with nocturnal respiratory symptoms or compliance to NIV treatment. Nocturnal capnography values were reliable and strongly correlated with the patients' respiratory symptoms (R(2) = 0.211-0.305, p = 0.004-0.021). **Author conclusions**: NC can be a efficient respiratory screening tool in a patient with ALS, and might be better than NPO in assessing nocturnal respiratory insufficiency and anticipating compliance to NIV treatment.
Cross-sectional	x		
Other (specify)			
Aim of study: To evaluate the efficacy of nocturnal capnography and nocturnal pulse oximetry **Data collection method:** Clinical tests **Sample size:** 26/38 **Identification/recruitment:** Unclear		Details of technology/NIV	
Lane 2015 **Journal paper / conference abstract** **Country: UK**		**Participant characteristics:** **Type of group** | Patients	**Data relating to NIV provision and usage:**

<table><tr><td>**RCT**</td><td></td></tr><tr><td>**Non-RCT**</td><td></td></tr><tr><td>**CBA**</td><td></td></tr><tr><td>**BA**</td><td></td></tr><tr><td colspan="2">**Comparator:**</td></tr><tr><td colspan="2">**Length of follow up:**</td></tr><tr><td>**Mixed method**</td><td></td></tr><tr><td>**Cross-sectional**</td><td></td></tr><tr><td>**Other (specify)**</td><td>Audit of casenotes</td></tr></table> **Aim of study:** To evaluate a domiciliary NIV service **Data collection method:** Satisfaction survey **Sample size:**18 **Identification/recruitment:** Patients accessing service	<table><tr><td>**Condition**</td><td>ALS</td></tr><tr><td>**Onset**</td><td>Not reported</td></tr><tr><td>**Sex**</td><td>Not reported</td></tr><tr><td>**Age**</td><td>Not reported</td></tr><tr><td>**NIV usage**</td><td>Not reported</td></tr><tr><td>**Other (specify)**</td><td></td></tr></table> Measures <table><tr><td>Satisfaction</td></tr></table> Details of technology/NIV <table><tr><td>Not reported</td></tr></table>	8 of 12 (67%) scored the service 10 (highly recommended) on the visual analogue scale, 4 patients left this blank. 100% responded that they had confidence and trust in the team and preferred to be seen at home. No adverse events were reported by these patients **Author conclusions**: MND patients requiring NIV can be safely and effectively managed in a home setting and find this preferable to hospital care.
Loewen 2014 **<u>Journal paper</u> / conference abstract** **Country: Canada** <table><tr><td>**RCT**</td><td></td></tr><tr><td>**Non-RCT**</td><td></td></tr><tr><td>**CBA**</td><td></td></tr><tr><td>**BA**</td><td></td></tr><tr><td colspan="2">**Comparator:**</td></tr><tr><td colspan="2">**Length of follow up:**</td></tr><tr><td>**Mixed method**</td><td></td></tr><tr><td>**Cross-sectional**</td><td></td></tr><tr><td>**Other (specify)**</td><td>Case note review</td></tr></table> **Aim of study:** To explore the value of split-night polysomnography	**Participant characteristics:** <table><tr><td>**Type of group**</td><td>Patients</td></tr><tr><td>**Condition**</td><td>ALS</td></tr><tr><td>**Onset**</td><td>Unclear</td></tr><tr><td>**Sex**</td><td>Unclear</td></tr><tr><td>**Age**</td><td>Unclear</td></tr><tr><td>**NIV usage**</td><td>Unclear</td></tr><tr><td>**Other (specify)**</td><td></td></tr></table> measures <table><tr><td>Completion of test</td></tr></table> Details of technology/NIV <table><tr><td>Not provided</td></tr></table>	**Data relating to NIV provision and usage:** Forty-three percent of patients had an incomplete test, resulting in a recommendation to repeat the polysomnogram. Poor sleep efficiency and absence of REM sleep in the diagnostic portion of the study were strongly associated with incomplete studies. Clinical variables that reflect severity of ALS (FVC, PaCO2, ALSFRS-R) and use of REM-suppressing antidepressants or sedative-hypnotics were not associated with incomplete split-night polysomnogram

<table>
<tr>
<td>Data collection method: Review of test data
Sample size: 47
Identification/recruitment: All eligible</td>
<td></td>
<td>Author conclusions:
A single, split-night polysomnogram is frequently inconclusive for the assessment of nocturnal hypoventilation and complete titration of non-invasive positive pressure ventilation in patients with ALS.</td>
</tr>
<tr>
<td>Lopes 2009/2012
<u>Journal paper</u> / conference abstract
Country: Portugal
<table>
<tr><td>RCT</td><td>X</td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To compare the cost of telemetry monitoring of NIV to standard care
Data collection method: Unclear
Sample size:39
Identification/recruitment: Unclear</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>13 bulbar, 27 spinal</td></tr>
<tr><td>Sex</td><td>27 male</td></tr>
<tr><td>Age</td><td>Average 61</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Cost of transport, office visits, maintenance of equipment

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
NHS costs evaluation showed a 55% reduction on average total costs (G1: 19,665 +/- 23,507 versus G2: 8,909 +/- 4,619; P = 0.05) with a statistically significant decrease of 81% on annual costs (G1: 44,134 +/- 50,607 versus G2: 8,186 +/- 6,553; P = 0.005) in G2.
Hospital costs were found to be significantly higher in G2 regarding to the total costs (64% average increase, P = 0.008) but not annual costs (7% average increase, P = 0.36).
No statistical difference was found concerning caregiver expenses from abseentism due to office visits or hospitalizations (P = 0.15
Author conclusions: The telemonitoring instrument proved to be cost-effective representing major cost savings to the NHS in the order of 700,000 per year.</td>
</tr>
<tr>
<td>Martinez 2015
<u>Journal paper</u> / conference abstract
Country: Spain
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
</table>
</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
In those subjects in whom, despite effective nocturnal NIV, symptoms of hypoventilation, hypercapnia, or respiratory accessory muscle use</td>
</tr>
</table>

CBA	
BA	
Comparator:	
Length of follow up: Unclear	
Mixed method	
Cross-sectional	
Other (specify)	**Cohort**

Aim of study: To explore tolerance
Data collection method: Respiratory testing in hospital
Sample size: 87
Identification/recruitment: All stable patients recruited

Age	
NIV usage	
Other (specify)	

Measures

Spirometry
Cough peak flow,
maximum insufflation capacity,
manually mechanically assisted cough peak flows were assessed
with a sealed oronasal mask
overnight pulse oximetry
Arterial blood gases

Details of technology/NIV

Portable ventilator in the VC-CMV mode (PV 501 and PV 403, Breas Medical, Moln-lycke, Sweden; AiroxHome2 and Legendair, Airox, Pau, France).

Ventilator adjustments were performed in the hospital during nocturnal cardiorespiratory monitoring. NIV was delivered through oronasal masks (Mirage, ResMed, Madrid, Spain), lip-seal mouthpiece (Tyco-Puritan Ben-nett, Pleasanton, California), or nasal interfaces (Health-dyne, Marietta, Georgia) during the night to optimize comfort and minimize air leaks. The ventilator was initially

persisted, daytime NIV was adjusted through a mouthpiece, lip-seal mouthpiece, or nasal pillow interfaces, as needed.
In those subjects with cough peak flow levels <4.25 L/s, mechanically assisted coughing was prescribed.
All subjects received therapeutic procedures (multidisciplinary care, scheduled clinical assessments, nutritional support, psychological management, neurological treatment, and sialorrhoea treatment) in accordance with expert guidelines. A clinical and functional assessment was scheduled every 3 months.
The causes for poor tolerance reported by subjects were: problems related to the interface in one subject, refusal of NIV treatment by 3 subjects, and episodes of sudden breathlessness during NIV in 3 subjects. Despite changes in masks and ventilator parameters and transfer to PC-CMV-NIV tolerance did not improve.
Tracheostomy considered if NIV could not provide adequate alveolar ventilation, when cough assistance could not remove airway secretions or patient preference.
Author conclusions: Patients who presented a lower cough peak flow generated with mechanically assisted coughing and more time spent with SpO2 below 90% during NIV at night were more likely to

<table>
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<td>adjusted to obtain a tidal volume of around 10 mL/kg, an inspiratory-expiratory ratio of 1:1.2 or 1:1.5, a backup breathing frequency near that of spontaneous breathing, and an inspiratory trigger sensitivity of -0.5 cm H2O.

Settings were readjusted during the night based on the subjects' comfort levels to achieve effective ventilation. Ventilation was considered to be effective when the percentage of time spent with SpO2 on NIV was <90% at night on NIV was less than 5%, the PaCO2 while on NIV was <45mm Hg, and hypoventilation symptoms were avoided.</td>
<td></td>
<td>have low adherence.
There was no relationship between bulbar dysfunction and NIV tolerance.</td>
</tr>
<tr>
<td>McKim 2012
<u>Journal paper</u> / conference abstract
Country: Canada
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort study</td></tr>
</table>
Aim of study: To evaluate an education programme for ALS patients and carers
Data collection method:</td>
<td>Participant characteristics:
Measures
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>8 male, 18 female</td></tr>
<tr><td>Age</td><td>Average 63</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table></td>
<td>Data relating to NIV provision and usage:
Single group education session led by respiratory therapist
Found a significant reduction in the uncertainty by patients about ventilatory decisions from 75% to 4%, and for their caregivers from 65% to 24%.

Author conclusions:
Instead of awaiting the onset of respiratory failure, this educational intervention allowed advanced discussion of ventilatory choices by patients and their caregivers and resulted in the mechanical ventilation of only those who desired it.
A formal ventilation patient</td>
</tr>
</table>

<table>
<tr>
<td>Questionnaires
Sample size: 26 patients, 26 carers
Identification/recruitment:
Approached at a clinic visit</td>
<td>The ALS Education Programme Questionnaire for patients with ALS and The ALS Education Programme Questionnaire for caregivers

Details of technology/NIV
Invasive and NIV</td>
<td>education programme is of benefit in respecting patients' wishes and fully informing a critical decision-making process.</td>
</tr>
<tr>
<td>Melo 1999
<u>Journal paper</u> / conference abstract
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To evaluate standards of care
Data collection method: Postal survey
Sample size: 20 centres
Identification/recruitment: Posted to Directors of 48 centres</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Specialist centres</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>N/A</td></tr>
<tr><td>Sex</td><td>N/A</td></tr>
<tr><td>Age</td><td>N/A</td></tr>
<tr><td>NIV usage</td><td>N/A</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Reported practice

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
Pulmonary function tests were performed at each visit in 17/20 institutions. Arterial blood gases, maximal expiratory pressures and maximal inspiratory pressures were followed in three centres and serum chloride was monitored in four centres.
The use of non-invasive ventilation (NIV) was extremely variable (range 0-50%). The majority of centres used symptoms/signs of hypoventilation and worsening forced vital capacity (FVC) to initiate NIV with no established protocol. A FVC between 20 and 40% was used by most to initiate NIV.
Author conclusions:
There was considerable variation in practice</td>
</tr>
<tr>
<td>Morgan 2005
Journal paper / <u>conference abstract</u></td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
</table></td>
<td>Data relating to NIV provision and usage:</td>
</tr>
</table>

Country: Ireland

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up: 3 years	
Mixed method	
Cross-sectional	
Other (specify)	Cohort

Aim of study: To examine the value of SNIFF
Data collection method: Pulmonary function testing
Sample size: 98
Identification/recruitment: Unclear

Measures

FVC
SNIFF
Survival

Condition	ALS
Onset	Not reported
Sex	Not reported
Age	Not reported
NIV usage	Not reported
Other (specify)	

Details of technology/NIV

Not reported

Sniff nasal-inspiratory force correlated with the transdiaphragmatic pressure (r = 0.9, p < 0.01). Sniff nasal-inspiratory force was most likely to be recorded at the last visit (96% of cases), compared with either the FVC or mouth-inspiratory force (86% and 81%, respectively, p < 0.01). A sniff nasal-inspiratory force less than 40 cm H2O was significantly related with nocturnal hypoxemia. When sniff nasal-inspiratory force was less than 40 cm H2O, the hazard ratio for death was 9.1 (p = 0.001),
Author conclusions: **T**he sniff nasal-inspiratory force test is a good measure of respiratory muscle strength in amyotrophic lateral sclerosis, it can be performed by patients with advanced disease

Motor Neurne Disease Association 2015/2017
Grey literature
Country: UK

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Practice guidelines

Participant characteristics:

Measures

N/A

Type of group	Patients
Condition	ALS
Onset	
Sex	
Age	
NIV usage	
Other (specify)	

Details of technology/NIV

N/A

Data relating to NIV provision and usage:
2015 Information for patients on troubleshooting for NIV.
Highlights need for patients to be proactive in asking professionals to explain things. Need for cleaning the mask regularly or replacing inlet filters.
Whoever supplies your NIV equipment will provide contact details for help with any technical difficulty. This will include an out-of-office hours contact.
If you are dependent on NIV or using it more than 12 hours a day, ask your provider about a spare

Aim of study: N/A **Data collection method: N/A** **Sample size: N/A** **Identification/recruitment: N/A**		device to keep as back-up. Power failure - You may also wish to consider using a power generator. Your respiratory team or the equipment provider can advise. It can also help to speak to your energy provider about registering as a priority user. This means you should get reconnected as early as possible if there is a power cut. Ask your provider about a device that can be powered both by mains and battery. However, your respiratory team can answer questions and assist if you experience any direct discomfort with: • your face or eyes • your nose, mouth, or speech and communication • managing saliva and mucus, or chest infections • eating and drinking • anxiety or panic. The 2017 information sheet provides guidance on withdrawal 1: Why do I need to think about withdrawal of ventilation? 2: Who needs to be involved in discussions? 3: How is withdrawal of ventilation arranged? 4: What happens when ventilation is withdrawn? 5: What support can be provided? Extending life may be what you wish to happen. It may be something you want to avoid. Your views may change over time, but

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<td>being informed helps you feel prepared.
You can stop using ventilation at any point, if you wish, or continue using ventilation for as long as you want to – the choice is yours.
Becoming reliant means you will no longer be able to breathe effectively without the help of the machine, which means your life is at risk if you stop using it. Removal of ventilation in these circumstances is known as withdrawal and it can be helpful to understand how this would be managed.
Author conclusions:
Reading about withdrawal may feel difficult, but may help you make timely choices and communicate your wishes. As your illness progresses, the professionals working with you will help you review or revisit your decisions to consider if you are settled in your view.</td>
</tr>
<tr>
<td>Nicholson 2016
Journal paper / <u>conference abstract</u>
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
</table>
</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>32 female</td></tr>
<tr><td>Age</td><td>Mean 61</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td>At baseline mean FVC was 58.6</td></tr>
</table>
Measures
<table>
<tr><td>Not reported</td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
Overall, mean number of hours' use of NIV increased from 5.7 to 7.0 to 8.2 hours for visits 1, 2 and 3 respectively. At visit 1, 33 (37.5%) patients were using their NIV device for less than 4 hours per night. This decreased progressively to 21.6% by visit 2 and 16.1% by visit 3. Median time to second and third visits was 15 and 35 weeks respectively. Although the number</td>
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<table>
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<table>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>
Aim of study: To investigate the use of four hours use as indicating compliance
Data collection method: Unclear
Sample size: 90
Identification/recruitment: Unclear
</td>
<td>
Details of technology/NIV
<table><tr><td>Not reported</td></tr></table>
</td>
<td>
of patients using NIV for less than 4 hours decreased from visits 2 to 3 this was not statistically significant.

Author conclusions:
Patients may initially demonstrate poor compliance as defined by Medicare recommendations. However, over time this compliance is seen to improve significantly.
</td>
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<td>
Nicholson 2017
<u>Journal paper</u> / conference abstract
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Chart review</td></tr>
</table>
Aim of study: To explore the usefulness of recorded machine data
Data collection method: Machine data
Sample size: 271
Identification/recruitment: Unclear
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table><tr><td>Device-recorded data</td></tr></table>
Details of technology/NIV
<table><tr><td>Volume assured pressure support versus pressure support NIV</td></tr></table>
</td>
<td>
Data relating to NIV provision and usage:
Examination of device data for exhaled tidal volumes and f/VT may be of use in evaluating efficacy of NIV in ALS.
Volume assured pressure support provides more reliable goal tidal volume than does PS, and is associated with decreased rate of respiratory to tidal volume.
Spontaneous cycling is decreased in ALS despite preservation of triggering ability.
There was no association found between spontaneous triggering or cycling, and pulmonary function, indicating the presence of low spontaneous breath cycling or triggering ability is difficult to predict.

Author conclusions:
Although a set backup rate may address decreased triggering, perhaps more importantly, setting a sufficient fixed inspiratory time would address the issue of decreased cycling.
</td>
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</table>

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<tr>
<td></td>
<td></td>
<td>Examination of device data for exhaled tidal volumes and f/VT may be of use in evaluating efficacy of NIV in ALS.</td>
</tr>
<tr>
<td>Nixon 2015/Oliver 2015
<u>Journal paper</u> / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Service evaluation</td></tr>
</table>
Aim of study: Evaluate a joint clinic for palliative and respiratory care
Data collection method: Unclear
Sample size: 13
Identification/recruitment: All seen over 3 year period</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>9 male 4 female</td></tr>
<tr><td>Age</td><td>Mean 57</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table>
<tr><td>Description</td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>Not reported</td></tr>
</table></td>
<td>Data relating to NIV provision and usage:
12 patients started on NIV successfully at home; 15% of all the patients are cared for with MND/ALS in the area with repeated visits and support from the Specialist Respiratory Nurse, facilitating the use of NIV for patients who were initially very anxious
Two were withdrawn from NIV at their request and the others died without needing withdrawal.
Author conclusions:
This joint approach has allowed people with MND/ALS to start NIV, with improvement in quality of life. The discussion has allowed a wider consideration of the benefits of NIV and the discussion of disease progression and the possible consideration of later withdrawal, as recommended by the NICE Guidance. The joint clinic has allowed a clearer approach to patient care with home commencement of NIV with a more comprehensive service.</td>
</tr>
<tr>
<td>O Neil 2012
<u>Journal paper</u> / conference abstract
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
</table></td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
</table></td>
<td>Data relating to NIV provision and usage:
38% of responding neurologists assessed respiratory function at presentation and 20% routinely</td>
</tr>
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<table>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study:
Data collection method: Postal survey
Sample size: 612 patients, unclear how many neurologists
Identification/recruitment: Responders
</td>
<td>
<table>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
NIV use
Service provision

Details of technology/NIV
Not reported
</td>
<td>
monitored respiratory function; 32% relied on symptoms as the only criterion for NIV referral and 43% used a combination of symptoms and physiological impairment.
75% of responding neurologists accessed specialist palliative care services for their patients towards the end of life and 69% at an earlier stage.

Author conclusions:
The proportion successfully established on NIV has increased, suggesting more appropriate selection and/or improvement in the methods of using NIV.
Monitoring of respiratory function is suboptimal and uncontrolled oxygen is sometimes used inappropriately before the terminal phase.
</td>
</tr>
<tr>
<td>
Oliver 2011
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
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</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Usage
Views

Details of technology/NIV
</td>
<td>
Data relating to NIV provision and usage:
non-invasive ventilation usage varied from 10% to 50% with a mean of 18%.Consultants in palliative medicine were concerned that the interventions could lead to distress to patients and families if they were used inappropriately and without clear discussion beforehand. There was need to provide clear and helpful information for patients and families and for the discussion to take place over a period of time, as a
</td>
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</table>

<table>
<tr>
<td>Aim of study: To ascertain the use of the interventions in several hospices and the attitudes of consultants in palliative medicine across the country to the use of PEG and NIV
Data collection method: Telephone questionnaire, case note audit
Sample size: 60
Identification/recruitment: Patients who had died at hospices</td>
<td>Not reported</td>
<td>"process" rather than on a single occasion.

Author conclusions:
There is limited involvement in the decision making for interventions that may promote quality of life and potentially extend life. These decisions may occur before hospice teams are involved and there are concerns that the information provided for patients and families may not always be adequate. The study shows that there may be a need for specialist palliative care teams to be working in a more collaborative way.</td>
</tr>
<tr>
<td>Oliver 2016
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up: 5 months</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>
Aim of study: To identify any trends in pressure support and hours of use of AVAPS ventilation in patients commencing NIV
Data collection method: Survey +</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>5 male 1 female</td></tr>
<tr><td>Age</td><td>Median 46</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Patient report, machine data

Details of technology/NIV
AVAPS-AE (Average volume assured pressure support - auto end positive airway pressure)
Monitoring of NIV using a modem</td>
<td>Data relating to NIV provision and usage:
The average use - 7h 28 min at one month rising to 9h 1 min at three months - and compliance - percentage greater than 4 h 75% at 1 month to 87% at 3 months; did show a positive trend, however, this did not reach significance.

Author conclusions:
There is an increase in average hours of use and compliance in the first 3 months of use and pressure support appears to increase over time.</td>
</tr>
</table>

<table>
<tr>
<td>machine data
Sample size: 6
Identification/recruitment: Unclear</td>
<td>attached to the ventilator
Patients used different devices including hand-held, mouthpiece and facemask breathing devices.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oliver 2016
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Review</td></tr>
</table>
Aim of study: To report a review undertaken by a guideline group
Data collection method: Literature review including RCTs and cohort studies and expert consensus
Sample size: N/A
Identification/recruitment: N/A</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>N/A</td></tr>
<tr><td>Sex</td><td>N/A</td></tr>
<tr><td>Age</td><td>N/A</td></tr>
<tr><td>NIV usage</td><td>N/A</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Any

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
A clinic based multidisciplinary approach should be used, allowing regular assessment of the patient and their needs psychological and social aspects should be considered regularly.
The person with MND should be offered the opportunity to discuss their concerns about the end of life particularly at diagnosis, if there are significant changes in their condition or if interventions are planned.
Equipment should be provided in a timely way, and should be able to be adaptable to cope with deterioration in the patient's abilities regular assessment of respiratory function is essential.
Author conclusions:
The comprehensive clinic based multidisciplinary approach effectively supports MND patients and families</td>
</tr>
<tr>
<td>Oliver 2018/2016
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
</table>
</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>Male</td></tr>
<tr><td>Age</td><td>Mean 55</td></tr>
<tr><td>NIV usage</td><td></td></tr>
</table>
</td>
<td>Data relating to NIV provision and usage:
There were problems as the pressures were not the same as they received with the NIV but they still found it worthwhile, and helped them maintain their independence.</td>
</tr>
</table>

Comparator: **Length of follow up:** **Mixed method** **Cross-sectional** X **Other (specify)** **Aim of study:** To evaluate use of a hand held ventilator **Data collection method:** Questionnaire **Sample size:** 3 (2 with ALS) **Identification/recruitment:** Unclear	**Other (specify)** NIV use 10-22 hours per day Measures Patient report Details of technology/NIV Vitabreath (Philips Responics)	**Author conclusions**: The use of a hand held ventilator Vitabreath is useful in supporting patients who are becoming more dependent on NIV. in what seems a more normal way than resorting to using the NIV.
Onders 2013 **Journal paper / <u>conference abstract</u>** **Country: UK** **RCT** **Non-RCT** **CBA** **BA** **Comparator:** **Length of follow up:** **Mixed method** **Cross-sectional** **Other (specify)** Analysis of a database **Aim of study:** Analyse patients with FVC's greater than 65% or less than 45% to determine the relationship between FVC and other diaphragm functional tests **Data collection method:** **Sample size:** 96 + 86 patients using	**Participant characteristics:** **Type of group** Patients **Condition** ALS **Onset** **Sex** **Age** **NIV usage** **Other (specify)** 24 FVC 45% or less, 29 FVC above 65% Measures Phrenic nerve conduction study SNIFF Details of technology/NIV N/A	**Data relating to NIV provision and usage:** Sniff fluoroscopy of diaphragm function had the greatest correlation to MIP (r = 0.47) then CO 2 levels (r = 0.33) then FVC with the weakest (r = 0.29). **Author conclusions**: ALS patients need a thorough analysis of diaphragm function to assist in prognosis and management of their disease. In ALS, a FVC above 65% is considered adequate yet many can have considerable diaphragm dysfunction.

<table>
<tr>
<td>diaphragm pacing
Identification/recruitment:</td>
<td></td>
<td></td>
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<tr>
<td>Oreja-Guevara 2012
Journal paper / <u>conference abstract</u>
Country: Spain
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To explore views of interventions
Data collection method: Survey
Sample size: 30 patients, 30 carers, 30 physicians
Identification/recruitment: Unclear</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Mean 56</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Views

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
All doctors agree to use NIPPV in all patients and situations
50% of patients agree with the opinion of physicians and caregivers
Only 20% of patients accepted IMV, like the caregivers and doctors.
Physicians showed very different opinions: from acceptation to rejection of IMV.

Author conclusions:
The perception of the patients, caregivers and doctors in relation to PEG, IMV and NIPPV is very different.</td>
</tr>
<tr>
<td>Palmer 2009/2011
<u>Journal paper</u> / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Case note review</td></tr>
</table>
</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS and COPD</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Concordance, drop out</td>
<td>Data relating to NIV provision and usage:
Mean length of stay for inpatient set-up was 6.7 days (range 1-30). Up to 450 bed-days were therefore saved as a result of domiciliary initiation. Overall concordance rate was 84.1% (n= 111) with little difference in dropout rate between home and hospital initiation (17.3% (n=12) vs 14.2% (n = 9)), similar to existing data for the outpatient department (82% concordance) and hospital initiation (75% and 97% concordance).</td>
</tr>
</table>

<table>
<tr>
<td>Aim of study: To compare home versus in patient initiation
Data collection method: Case note review and analysis of survey
Sample size: 132
Identification/recruitment: Unclear</td>
<td>Details of technology/NIV
Not reported</td>
<td>While in hospital, those with motor neurone disease (MND) failed most frequently. Interestingly, patients with MND had excellent domiciliary success with only 8% (n= 2) being non-concordant. Non-concordance does not appear to be strongly linked to support at home. Inpatient set-up slightly favoured concordance in those who lived alone (81% vs 71%). All patients initiated in 2007-8 agreed or strongly agreed that they felt well supported by the service. Those being set up at home showed a greater tendency to strongly agree rather than just agree (75% vs 67%)
Author conclusions:
Establishing NIV at home can be appropriate even for those with marked ventilatory failure. It does not affect concordance and supports patients while having the added advantage of decreasing bed usage and costs.</td>
</tr>
<tr>
<td>Panchabhai 2016
Journal paper / <u>conference abstract</u>
Country: USA
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
</table>
</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
FVC</td>
<td>Data relating to NIV provision and usage:
At NIPPV initiation, the vital capacity was 46% in both those who went on to be tolerant versus those who were not. The indication for slope of FVCP decline was 1.1% per month in intolerant versus 1.5% per month in tolerant subjects. Decline of FVCP starts later but is more rapid in patients with subsequent adherence to NIPPV. By the time NIPPV is initiated,</td>
</tr>
</table>

<table>
<tr>
<td>
<table>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>
Aim of study: To model the course of lung function decline
Data collection method: Unclear
Sample size: 515
Identification/recruitment: Unclear
</td>
<td>
Details of technology/NIV
<table><tr><td>Not reported</td></tr></table>
</td>
<td>
subjects have already lost about 85% of the expected range of lung function.

Author conclusions:
Guidelines for the FVCP threshold for initiation of NIPPV in patients with ALS may need to be revised to assess whether earlier NIPPV has an impact on lung function.
</td>
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<td>
Park 2017
Journal paper / <u>conference abstract</u>
Country: South Korea
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Case studies</td></tr>
</table>
Aim of study: To investigate different pressure mode settings
Data collection method: Unclear
Sample size: 3
Identification/recruitment: Unclear
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>Not reported</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td>With respiratory difficulty</td></tr>
</table>
Measures
<table><tr><td>Descriptive</td></tr></table>
Details of technology/NIV
<table><tr><td>Not reported</td></tr></table>
</td>
<td>
Data relating to NIV provision and usage:
Case 1 shows that the VCV mode may have an advantage in managing respiratory insufficiency of patients in situations where the inner diameter of the airway decreases because of increased sputum. In contrast, cases 2 and 3, show that changing to the PCV mode may be one of the treatment options if not enough tidal volume can be supplied to resolve respiratory insufficiency because of an increase in leakage volume.

Author conclusions:
Clinical symptoms were improved by changing ventilation mode,
</td>
</tr>
<tr>
<td>
Parker 2009
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
</table>
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>11 bulbar</td></tr>
<tr><td>Sex</td><td>9 male</td></tr>
<tr><td>Age</td><td>Mean 65</td></tr>
<tr><td>NIV usage</td><td></td></tr>
</table>
</td>
<td>
Data relating to NIV provision and usage:

Oxygen saturation, VC and arterial blood gases were measured in all respiratory clinic attendees. Symptoms of hypoventilation and
</td>
</tr>
</table>

Comparator: **Length of follow up:** **Mixed method** **Cross-sectional** **Other (specify)** Case note review **Aim of study:** To explore predictors of success **Data collection method:** Examination of notes **Sample size:**21 **Identification/recruitment:** Unclear	**Other (specify)** 8 needed urgent NIV Measures Descriptive Details of technology/NIV Not reported	daytime sleepiness were incompletely documented, particularly in neurology clinic letters, and Epworth score was never measured. Ten underwent sleep studies. 57% had a VC below which NIV should be considered, with the majority in daytime ventilatory failure. **Author conclusions**: Many patients were referred late in their disease trajectory. Most were seen only once in the respiratory clinic before needing to start NIV. Those successfully starting NIV had better VC, non-bulbar MND, elective set-up and less chronic ventilatory failure than those discontinuing NIV
Peysson 2008 **Journal paper** / **conference abstract** **Country:** France **RCT** **Non-RCT** **CBA** **BA** **Comparator:** **Length of follow up:** **Mixed method** **Cross-sectional** Retrospective analysis **Other (specify)** **Aim of study:** To determine factors predicting survival	**Participant characteristics:** **Type of group** Patients **Condition** ALS **Onset** 10 bulbar **Sex** **Age** **NIV usage** Median usage 10-14 hours per day **Other (specify)** Measures Median survival Details of technology/NIV Not reported	**Data relating to NIV provision and usage:** Survival worsened with age and bulbar symptoms **Author conclusions**: Age and secretion accumulation affect prognosis but NIV is useful for all patients including those with bulbar symptoms

<table>
<tr>
<td>Data collection method: Case notes
Sample size:33
Identification/recruitment:
Consecutive</td>
<td></td>
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</tr>
<tr>
<td>Piggin 2009
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td>X</td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To evaluate validity of the Epworth Sleepiness scale
Data collection method: Evaluated prior to NIV and 3 months after
Sample size:7
Identification/recruitment: Unclear</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>6 male</td></tr>
<tr><td>Age</td><td>Mean 66</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Pulse oximetry
The ESS
Views and perceptions

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
Patients reported substantial improvement in sleep quality and reductions in daytime somnolence beyond those suggested by change in ESS scores
Pre-NIV, 3 patients scored >=10 on ESS (range 2-17; M = 8.0). Pre-NIV ESS scores correlated significantly with percentage time <saturation in pre-NIV oximetry (M = 21.22%, SD = 22.06; r = 0.786, p = 0.036). However, ESS scores did not correspond to individual qualitative experiences, underestimating symptom severity.
Post-NIV, ESS scores (range 1-12; M = 6.29) did not differ significantly from pre-NIV scores (t (6) = 0.61, p = 0.56) and did not correlate with any post-NIV oximetry markers. The trend in ESS scores towards decreased sleepiness (M= 0.29, SD= 7.65) following NIV initiation did significantly correlate with the change in percentage time spent <saturation (M = 16.8, SD = 13.24; r = 0.841, p = 0.018).
Author conclusions: The scale did not accurately capture the significant improvement in sleepiness reported by patients.</td>
</tr>
<tr>
<td>Pinto 2003</td>
<td>Participant characteristics:</td>
<td>Data relating to NIV provision</td>
</tr>
</table>

<table>
<tr>
<td>
<u>Journal paper</u> / conference abstract
Country: Portugal
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td>X</td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator: Historical group</td></tr>
<tr><td colspan="2">Length of follow up: Every 3 months until death</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To explore the optimal time for introduction of NIV
Data collection method: unclear
Sample size: 64 (42 in analysis)
Identification/recruitment: Consecutive
</td>
<td>
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>18 bulbar</td></tr>
<tr><td>Sex</td><td>22 female, 42 male</td></tr>
<tr><td>Age</td><td>Mean age 60 & 56</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Nocturnal respiratory events measured by pulse oximetry
Survival
FVC
Blood gases
Norris score

Details of technology/NIV
Vitalograph1 (Respironics) and Pulsox1 (Minolta) oximeters
</td>
<td>
and usage:
Total survival, and survival with NIV, were longer in Group 2 (p,0.01), in which an early introduction of NIV was made. No relationship was found between time to NIV and total survival.

Author conclusions:
NPO is useful tool to establish need for NIV. NPO is a low cost and simple screening method for assessing ALS patients.
Early use of NIV increases compliance.
Clinical characteristics and conventional RFT are inadequate as criteria for NIV initiation.
</td>
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<td>
Pinto 2010
Journal paper / <u>conference abstract</u>
Country: Portugal
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2"><u>Length of follow up:</u> Before</td></tr>
</table>
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>57 bulbar</td></tr>
<tr><td>Sex</td><td>59 female</td></tr>
<tr><td>Age</td><td>Mean 61 at onset</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
</td>
<td>
Data relating to NIV provision and usage:

Mean PhrenAmpl is a non-volitional respiratory test which is strongly predictive of the need for NIV in ALS patients.
The following covariates were predictive of NIV: late onset (P = 0.027), low ALS-FRS (P = 0.027),
</td>
</tr>
</table>

and after NIV **Mixed method** **Cross-sectional** **Other (specify)** Cohort **Aim of study:** To evaluate the value of the phrenic nerve response **Data collection method:** Clinical tests **Sample size:** 138 of 469 **Identification/recruitment:** Consecutive	Mean PhrenAmpl FVC Details of technology/NIV Not reported	low FVC (P = 0.006), and low Mean PhrenAmpl (P < 0.001). Mean PhrenAmpl was significant for both groups (P < 0.001 and P = 0.071 for spinal and bulbar onset patients, respectively), **Author conclusions**: Motor unit loss in the diaphragm is a main factor determining respiratory symptoms in ALS. This test should be more extensively applied in this disease.
Pinto 2010 (linked to Ando 2016) **Journal paper / conference abstract** **Country:** Portugal **RCT** X **Non-RCT** **CBA** **BA** **Comparator:** **Length of follow up:** Span of NIV use **Mixed method** **Cross-sectional** **Other (specify)** **Aim of study:** To evaluate the value of use of a modem for telemonitoring **Data collection method:** Records of visits, monitoring data **Sample size:** 40 **Identification/recruitment:** Consecutive	**Participant characteristics:** **Type of group** Patients **Condition** ALS **Onset** **Sex** **Age** **NIV usage** **Other (specify)** Measures Number of visits Compliance, survival Details of technology/NIV Modem connection to NIV	**Data relating to NIV provision and usage:** No difference in compliance between groups. The number of office or emergency room visits and admissions was significantly lower in the intervention group (p<0.0001). Survival not significantly different between groups (p=0.13). **Author conclusions**: Telemonitoring reduces health care utilisation, may have a beneficial impact on costs.
Pinto 2017 **Journal paper / conference abstract**	**Participant characteristics:** **Type of group** Patients	**Data relating to NIV provision and usage:**

Country: Spain

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	x
Other (specify)	

Aim of study: To examine the degree of correlation between test scores
Data collection method: Clinical test
Sample size:592
Identification/recruitment: Consecutive

Measures

Revised ALS functional rating scale, ALSFRS respiratory (R-subscore) and bulbar subscores, SVC, FVC, Maximal inspiratory (MIP) and expiratory (MEP) pressures.

Condition	ALS
Onset	
Sex	332 male
Age	
NIV usage	
Other (specify)	

Details of technology/NIV

Not reported

FVC and SVC were strongly correlated. Both were strongly correlated with MIP and MEP and moderately correlated with R-subscore for the all population and spinal-onset patients, but weakly correlated for bulbar-onset patients.

Author conclusions:
FVC and SVC were strongly correlated and declined similarly. This correlation was preserved in bulbar-onset ALS.

Porcu 2013/2014
Journal paper / conference abstract
Country: Italy

RCT	
Non-RCT	

Participant characteristics:

Type of group	Patients
Condition	ALS
Onset	Not reported
Sex	Not reported

Data relating to NIV provision and usage:
Desaturation and periods of nocturnal hypoventilation during spontaneous breathing were easily

CBA		**Age**	Not reported
BA		**NIV usage**	Not reported
Comparator:		**Other (specify)**	
Length of follow up:			
Mixed method			
Cross-sectional			
Other (specify)	**Cohort**		

Aim of study: To explore the use of telemonitoring of NPO
Data collection method:
Sample size: 15
Identification/recruitment: Not reported

Measures

Time spent with a saturation below 90% (TB90%) for 35% of study time

Mean nocturnal saturation (MNS) for each recording

Details of technology/NIV

A telemonitoring device which acquires signals from an internal pulseoximeter and connects to a modem by bluetooth technology.

detected. The system enabled monitoring of changes in parameter settings of the ventilator during NIV adaptation

Author conclusions:
Home monitoring of NPO was found to be user-friendly by the patients. The system allowed the monitoring of nocturnal patterns of breathing and thereby assessment of NIV effectiveness.

Prell 2015/2016
Journal paper / conference abstract
Country: Germany

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	X
Other (specify)	

Aim of study: Comparison of different

Participant characteristics:

Measures

Type of group	Patients
Condition	ALS
Onset	
Sex	
Age	
NIV usage	
Other (specify)	

Data relating to NIV provision and usage:
The ALSFRS-R and its respiratory question correlated with the decline of VC, FCV and changes in nocturnal BGA. However, the absence of dyspnea doesn't rule out a relevant respiratory impairment, since 30% of the ALS patients not complaining of dyspnea had a FVC lower than 75% predicted.
The absence of nocturnal hypoventilation does not necessarily indicate normal respiratory function, since FVC

<table>
<tr>
<td>assessments of respiratory function
Data collection method: Review of clinical data
Sample size: 131
Identification/recruitment: Unclear</td>
<td>Respiratory polygraphy – pulse oximetry, oronasal pressure and flow, chest/abdomen movement, body position, SpO2
FVC
VC
MIP (Pimax)
ALSFRS-R

Details of technology/NIV
(Somnoscreen from SOMNO medics Randersacker,</td>
<td></td>
<td>ranges in this group from 25% till 123% of predicted.
Sleep related respiratory events were more common in the early stages of disease
The patient group with nocturnal hypoventilation was characterised by a significantly lower VC, FVC and maximal static inspiratory pressure compared with the group without nocturnal hypoventilation. However, also in the absence of nocturnal hypoventilation, 8 patients had a VC <50% as predicted.

Author conclusions:
Polygraphy does not provide useful additional information if the FVC is already <75% as predicted. However, in patients with more or less normal lung function parameters or where lung spirometry cannot be performed adequately (eg, bulbar ALS), it can provide sufficient evidence for the need of NPPV</td>
</tr>
<tr>
<td>Proctor 2013
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
</table>
</td>
<td>Participant characteristics:
Measures
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>72 male</td></tr>
<tr><td>Age</td><td>Mean 66</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td></td>
<td>Data relating to NIV provision and usage:
Bulbar status was not a significant factor (p = 0.112), but there did appear to be a trend for less survival benefit in those patients with bulbar symptoms. There was no effect shown with pCO2, age or sex.

Survival was significantly related to therapy compliance</td>
</tr>
</table>

Cross-sectional		Survival Compliance	**Author conclusions**: Patients with bulbar symptoms should be considered for a trial
Other (specify)	**X**		
Aim of study: To report on the use of NIV **Data collection method:** Routine data **Sample size:** 117 **Identification/recruitment:** Consecutive		Details of technology/NIV Not reported	
Rafiq 2012 **Journal paper / conference abstract** **Country:** UK	**Participant characteristics:** **Type of group**: Patients **Condition**: ALS **Onset**: Not reported **Sex**: Not reported **Age**: Not reported **NIV usage**: Not reported **Other (specify)**:		**Data relating to NIV provision and usage:** The partial pressure of CO2 was compared using both transcutaneous monitoring and by an arterialized ear lobe capillary blood sample. The mean difference between arterialized and transcutaneous readings was -0.083 kPa (SD 0.318).
RCT		Measures CO2 levels	**Author conclusions**: Monitoring using a TOSCA monitor is a useful clinical tool. There is a possibility of occasional inaccurate readings which should be verified with a blood gas analysis.
Non-RCT			
CBA			
BA			
Comparator:		Details of technology/NIV	
Length of follow up:			
Mixed method			
Cross-sectional	x		
Other (specify)			
Aim of study: To validate the accuracy of carbon dioxide level recorded transcutaneously with a TOSCA 500 monitor. **Data collection method:** Test monitoring **Sample size:** 40 **Identification/recruitment:** Consecutive			
Restepo 2012 **Journal paper / conference abstract** **Country:** USA	**Participant characteristics:** **Type of group**: Patients **Condition**: ALS		**Data relating to NIV provision and usage:** Humidification is recommended on

RCT		**Onset**	N/A	every patient receiving invasive mechanical ventilation. Active humidification through a heated ventilator is suggested for noninvasive mechanical ventilation, as it may improve adherence and comfort. Passive humidification through a heat and moisture exchanger is not recommended for noninvasive mechanical ventilation. The resistance and dead space of the HME may negate the effects of the noninvasive positive pressure and add additional work of breathing. Use of an HME is contraindicated in patients on NIV with large mask leaks, as the patient does not exhale enough tidal volume to replenish heat and moisture to adequately condition the inspired gas. **Author conclusions**: The paper provides detailed guidance regarding provision and settings for humidification.
Non-RCT		**Sex**	N/A	
CBA		**Age**	N/A	
BA		**NIV usage**	Not repoted	
Comparator:		**Other (specify)**		
Length of follow up:		Measures		
Mixed method		N/A		
Cross-sectional		Details of technology/NIV		
Other (specify)	Review	N/A		
Aim of study: To update a practice guideline **Data collection method:** Review **Sample size:** N/A **Identification/recruitment: N/A**				
Ritsma 2009/2010 **Journal paper / conference abstract** **Country:** Canada		**Participant characteristics:**		**Data relating to NIV provision and usage:** Symptoms of respiratory insufficiency, namely orthopnea (clinical significance rated at 9.00/10 +/- 1.48), dyspnea (8.27 +/- 1.95) and morning headache (7.55 +/- 1.21) are the most significant indicators for NIPPV initiation. Barriers to NIPPV utilization are patient intolerance (70% of centres)
RCT		**Type of group**	Specialist centres	
Non-RCT		**Condition**	ALS	
CBA		**Onset**		
BA		**Sex**		
Comparator:		**Age**		
Length of follow up:		**NIV usage**		
		Other (specify)		
		Measures		

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<table>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To report current practice regarding NIV
Data collection method:
Sample size: 15 centres surveyed
Identification/recruitment: Survey sent to centres
</td>
<td>
Details of technology/NIV
<table><tr><td></td></tr></table>
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<td>
and inaccessibility of respirologists and ventilation technologists (50% of centres).

Author conclusions:
More definitive NIPPV initiation criteria, emphasizing respiratory symptoms, and the attenuation of barriers to NIPPV us are required.
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<td>
Rodriguez 2012
Journal paper / <u>conference abstract</u>
Country: Spain
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To explore views regarding the use of NIV
Data collection method: Survey
Sample size: 90
Identification/recruitment: Four centres, detail unclear
</td>
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Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients/carers/physicians</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>76% patients male</td></tr>
<tr><td>Age</td><td>Patient mean 56</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table><tr><td>Views and perceptions</td></tr></table>
Details of technology/NIV
<table><tr><td>Not reported</td></tr></table>
</td>
<td>
Data relating to NIV provision and usage:
50% of patients agree with the opinion of physicians and caregivers regarding NIV
IMV was the most controversial procedure, only in 20% of patients accepted IMV like the caregivers and doctors. Physicians showed very different opinions: from acceptance to the rejection of this procedure.

Author conclusions:
The perception of the patients, caregivers and doctors in relation to IMV and NV is very different. Decisions should be taken by all together.
</td>
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<td>
Ruffell 2012/2013
<u>Journal paper / conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
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</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Professionals</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>N/A</td></tr>
<tr><td>Sex</td><td>N/A</td></tr>
<tr><td>Age</td><td>N/A</td></tr>
</table>
</td>
<td>
Data relating to NIV provision and usage:
Analyses found significant differences between medical and non-medical professionals ' views on their impressions of patients ' and carers ' understanding of the
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Comparator: **Length of follow up:** **Mixed method** **Cross-sectional** X **Other (specify)** **Aim of study:** To explore the perceptions of professionals about interventions **Data collection method:** Online survey **Sample size:** 166 professionals **Identification/recruitment:** Via online survey		**NIV usage** N/A **Other (specify)** Measures Views Details of technology/NIV Not reported		effects of NIV on symptoms and quality of life. 76% of medical staff believed that discussion about NIV should begin after diagnosis but prior to intervention, compared to 45% allied health professionals. 48% of allied health professionals believed discussion timing should be on an individual basis. When asked whether people with ALS have a clear idea of the effects of NIV on QoL, 29% of medical and 8% of allied health professionals disagreed with the statement. When asked whether carers of people with ALS have a clear idea of the effects of NIV on symptoms, 41% of medical and 23% of allied health professionals were uncertain. Nearly 58% of allied health professionals agreed or strongly agreed that carers are aware of the possible effects of NIV on the patient's QoL, whilst 58% of medical staff were uncertain. **Author conclusions**: Clinical experience may be a relevant factor when providing care for people who refuse palliative interventions. Different types of HCPs may hold dissimilar views on the provision of NIV.

Sancho 2014
Journal paper / **conference abstract**
Country: Spain

RCT	
Non-RCT	
CBA	
BA	
Comparator: Two different units	
Length of follow up:	
Mixed method	
Cross-sectional	X
Other (specify)	

Aim of study: To compare the effectiveness of the different ventilator modes - volume (Vol-NIV) or pressure-cycled (Pres-NIV) ventilation
Data collection method: Retrospective analysis of data
Sample size: 82 + 62
Identification/recruitment: Retrospective analysis

Participant characteristics:

Type of group	Patients
Condition	ALS
Onset	
Sex	
Age	
NIV usage	
Other (specify)	

Measures

Details of technology/NIV

Not reported

Data relating to NIV provision and usage:
No differences were found in survival from NIV initiation between Vol-NIV (median 15.00 (7.48-22.41) months) and Pres-NIV (median 15.00 (10.25-19.75) months, p = 0.533) patients
Effective NIV was achieved in 72.41% Vol-NIV patients and in 48.78% Pres-NIV patients (p < 0.001)
Ventilator mode (OR 12.066 (4.251-32.270), p < 0.001) and severity of bulbar dysfunction (OR 1.07 (1.011-1.133), p = 0.02) were the variables correlated with effective NIV.

Author conclusions:
Vol-NIV provides more effective ventilation, but Vol-NIV and Pres-NIV present similar survival in ALS. Effectiveness of NIV is related to the severity of bulbar dysfunction.

Schellas 2018
Journal paper / **conference abstract**
Country: Spain

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	X

Participant characteristics:

Type of group	Patients
Condition	ALS and neuromuscular disease
Onset	Not reported
Sex	Not reported
Age	Not reported
NIV usage	Not reported
Other (specify)	

Measures

Data relating to NIV provision and usage:
Fixed expiratory positive airway pressure was significantly correlated with AHI reduction (r=0.50; p<0.001). The inspiratory-expiratory pressure interval (PAP, n=191) showed inverse correlation with the apnoea-hypopnoea index change achieved in the first treatment night (r=-0.28; p<0.001). However, PAP and the effective pressure range between EPAP and

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Other (specify)	

Aim of study: To investigate links between masks and upper airway obstruction
Data collection method: Clinical data
Sample size:212
Identification/recruitment: Unclear
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<td>

Treatment-induced upper airway obstruction (TAO)

Details of technology/NIV

Oronasal interface
</td>
<td>

the highest inspiratory PAP achieved were not predictive of TAO. In patients with ALS, TAO was associated with better bulbar function.
Author conclusions:
Initiation of NIV using an oronasal interface may be associated with intermittent obstruction in a subset of patients. Since both EPAP and PAP appear to play a causative role, careful titration of ventilator settings is recommended.
</td>
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Sheers 2013/2014
Journal paper / conference abstract
Country: Australia

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Cohort

Aim of study: To evaluate an ambulatory model of NIV initiation
Data collection method: Routine data, clinical measures
Sample size:
Identification/recruitment: All referred to NIV
</td>
<td>

Participant characteristics:

Type of group	Patients
Condition	ALS
Onset	Not reported
Sex	Not reported
Age	Not reported
NIV usage	Not reported
Other (specify)	

Measures

Waiting time, Hospital length of stay, Adverse events Polysomnography data.

Details of technology/NIV
</td>
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Data relating to NIV provision and usage:
With the Day Admission model the median waiting time fell from 30 to 13.5 days ($p < 0.04$) and adverse events declined (4/17 pre- (three deaths, one acute admission) versus. 0/12 post-). Survival was also prolonged (median (IQR) 278 (51-512) days pre- vs 580 (306-1355) days post-introduction of the Day Admission model; hazard ratio 0.41, $p = 0.04$). Daytime $PaCO_2$ was no different. Sleep quality was poorer.

Author conclusions:
This model of care provided an efficient option for implementing NIV, with waiting time reduced by 19 days and a 24% reduction in adverse events. Efficacy of
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<td>This model involved a 4 hour stay including mask fitting, bedside titration of the spontaneous-timed mode bi-level pressure ventilator and education, with follow-up in-laboratory polysomnography titration and outpatient attendance.

VPAP III ST and ST-A, Resmed, San Diego USA</td>
<td></td>
<td>ventilation, as measured by daytime PaCO 2 was similar. Patients were commenced on ventilation more quickly once the decision to ventilate was made. The data suggest that once a decision to ventilate has been made, delays in commencing NIV are clinically important and that alternative models of implementation can be effective.</td>
</tr>
<tr>
<td>Sorg 2010
Journal paper / <u>conference abstract</u>
Country: Germany
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td>X</td></tr><tr><td>Other (specify)</td><td></td></tr></table>
Aim of study: To explore whether cognitive deficits influence treatment decisions
Data collection method: Clinical tests
Sample size:48 patients, 73 controls
Identification/recruitment: Not reported</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients & controls</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>Not reported</td></tr><tr><td>Sex</td><td>Not reported</td></tr><tr><td>Age</td><td>Not reported</td></tr><tr><td>NIV usage</td><td></td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
D2 attention test
Speech comprehension
Verbal memory

Details of technology/NIV
N/A</td>
<td>Data relating to NIV provision and usage:

No differences were found in speech comprehension as well as verbal fluency between controls and patients.

Author conclusions:
We found no evidence for an association between cognitive impairment and decisions in favour of life sustaining treatment. This implies that patients with mild cognitive deficits may well be able to make adequate decisions on this matter.</td>
</tr>
<tr>
<td>Stewart 2001
<u>Journal paper</u> / conference abstract</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr></table></td>
<td>Data relating to NIV provision and usage:</td>
</tr>
</table>

Country: Canada

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Review of records

Aim of study: To examine the value of EMG
Data collection method: Clinical tests
Sample size:52
Identification/recruitment: All eligible patients

Condition	ALS
Onset	Not reported
Sex	Not reported
Age	Not reported
NIV usage	Not reported
Other (specify)	

Measures

Diaphragmatic EEG
FVC
Survival
Daytime arterial PO(2)

Details of technology/NIV

N/A

Patients with abnormal diaphragmatic EMG at diagnosis had significantly lower forced vital capacity (FVC), lower daytime arterial PO(2) and higher PCO(2) measurements ($p<0.05$) than patients with normal diaphragmatic EMG (Group 2, n=29). Twenty-eight percent of the patients without symptoms or signs of respiratory insufficiency at the time they were examined had an abnormal diaphragm EMG.
Treated patients (with abnormal diaphragm EMG) survived significantly longer ($p<0.05$) than untreated patients. They also started NIPPV earlier than treated patients without abnormal EMG.
Author conclusions:
Respiratory muscle EMG was simply and safely performed on ALS patients at or around the time of diagnosis. The procedure can detect sub-clinical respiratory muscle dysfunction.

Sugie 2006
Journal paper / conference abstract
Country: Japan

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	

Participant characteristics:

Type of group	Patients
Condition	ALS
Onset	Not bulbar
Sex	Male
Age	47
NIV usage	Pre-usage
Other (specify)	

Measures

Data relating to NIV provision and usage:

His pulmonary function tests and arterial blood gas analysis showed no abnormalities, but polysomnography (PSG) revealed sleep-disordered breathing requiring mechanical support ventilation. Bi-level positive airway pressure treatment was started only at night, which improved both sleep-disordered breathing and

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<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Case study</td></tr>
</table>
Aim of study: To report a case
Data collection method: Clinical tests
Sample size:1
Identification/recruitment: N/A
</td>
<td>
Pulmonary function tests
Blood gas analysis

Details of technology/NIV
Not reported
</td>
<td>
daytime activity.
Author conclusions:
PSG should be considered in ALS patients at an early clinical stage in order to predict mild respiratory dysfunction.
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<td>
Tamplin 2017
<u>Journal paper</u> / conference abstract
Country: Australia
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up: 3 months</td></tr>
<tr><td>Mixed method</td><td>X feasibility</td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To explore the usefulness of music therapy in NIV initiation
Data collection method:
Sample size: 15
Identification/recruitment: Unclear
</td>
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Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Anxiety
Quality of life
Views and perceptions

Details of technology/NIV
Not reported
</td>
<td>
Data relating to NIV provision and usage:
15 of 18 individuals choose the music therapy. Qualitative data indicated most participants considered the relaxing and distracting effects of music assisted relaxation was useful.
There were differing experiences of using the approach, and there were technical and logistical issues regarding timely and accessible provision within the treatment trajectory of NIV implementation.

Author conclusions:
Results suggested that supporting NIV transition within the first 7 days may be advantageous for long-term adherence. No effects were found for anxiety or quality of life.
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Terzano 2015
<u>Journal paper</u> / conference abstract
Country: Italy
<table>
<tr><td>RCT</td><td></td></tr>
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Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
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Data relating to NIV provision and usage:
PEF and FEV indicated worsening of lung function. PImax detected
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<table>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td>X</td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator: Those refusing NIV at early stage but started later as symptoms worsened versus those who accepted</td></tr>
<tr><td colspan="2">Length of follow up: 4 months</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To examine the efficacy of an early start of NIV
Data collection method: Clinical tests
Sample size: 36
Identification/recruitment:
Consecutive
</td>
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<table>
<tr><td>Sex</td><td>Just over half male</td></tr>
<tr><td>Age</td><td>Mean 63</td></tr>
<tr><td>NIV usage</td><td>Not reported</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Blood gases
FVC
Total lung capacity
PImax

Details of technology/NIV
Adaptation to ventilation and adjustment of ventilator settings were always done during an inpatient admission. The type of ventilator and interface were selected based on the patient's comfort and adaptation, correction of gas-exchange abnormalities and the number of hours of ventilation. Equipment used included volumetric ventilator (PV 501, BREAS Medicals, Mölnlycke, Sweden) or pressure ventilator (BiPAPST30 "auto-trak" ventilator, Respironics Inc, Murrysville, PA, USA). Interfaces included custommolded and commercial nasal masks with chin-strap to minimize oral leaks.
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<td>
worsening muscle strength and correlated with VC, indicating the importance of VC, FEV, and PImax as predictors for decline of lung function.
At the end of follow-up (Time 4), there was a worsening of the ventilatory capacity and arterial blood gas values in all patients, but, there was a significant worsening of Group B compared to Group A.
Unclear the timing of when those who delayed started or at what point the "early starters" were initiated.

Author conclusions:
Early start of NIV is important in order to postpone the function decline and the decrease of respiratory muscle strength
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Tilanus 2017
<u>Journal paper</u> / conference abstract
Country: Netherlands
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<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
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<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
</table>
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<td>
Data relating to NIV provision and usage:
The NIV indication was based on complaints of hypoventilation and/or proven (nocturnal) hypercapnia.
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CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Analysis of case records

Aim of study: To explore which tests predict need for NIV
Data collection method: Clinical tests
Sample size: 110
Identification/recruitment: N/A

Measures

FVC
Peak cough flow (PCF),
Maximum inspiratory and expiratory pressure (MIP and MEP)
Sniff nasal inspiratory pressure (SNIP)

Details of technology/NIV

Before referral to a home ventilation service, patients are, on average, tri-monthly monitored by one of the multidisciplinary ALS care teams. A referral to an HVS is indicated when one or more of the following occurs: FVC <70%, symptoms of nocturnal hypoventilation, signs of increased breathing activity or daytime

Age	
NIV usage	87 were recommended for NIV, 77 were successful users, 4 chose tracheostomy
Other (specify)	

SNIP showed the greatest decline within the latest 3 months before NIV indication (mean = −22%). PCF at the time of referral to the HVS significantly discriminated between the groups 'NIV-indication' and 'no NIV-indication yet' patients at the first HVS visit: 259 (±92) versus 348 (±137) L/min, p = 0.019. PCF and SNIP showed the best predictive characteristics in terms of sensitivity.

Author conclusions:
PCF significantly differentiated 'NIV-indication' from 'no NIV-indication yet' patients with ALS. Currently used cut-off values might be adjusted and other respiratory function tests such as SNIP and PCF may become part of routine care in patients with ALS in order to avoid non-timely initiation of (non-invasive) ventilation.

<table>
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<td>hypercapnia (PCO2 > 45 mmHg).
Other respiratory parameters, such as PCF or SNIP, are used infrequently in ALS clinics in Netherlands.
The NIV indication is based on either proven nocturnal or daytime hypercapnia, orthopnoea and/or other complaints of nocturnal or daytime hypoventilation</td>
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<td>Trail 2003
<u>Journal paper</u> / conference abstract
Country: USA
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td>X</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Aim of study: To compare patient and carers attitudes towards treatment options
Data collection method:
Questionnaire
Sample size: 27 patients and 19 carers
Identification/recruitment:
Consecutive</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>Not reported</td></tr><tr><td>Sex</td><td>Not reported</td></tr><tr><td>Age</td><td>Mean 56</td></tr><tr><td>NIV usage</td><td>Not reported</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
Views and perceptions

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
Patient and caregiver responses to the use of BIPAP differed. Though over half of both groups endorsed the idea of future BIPAP use, more patients (41%) than caregivers (5%) were uncertain. Only 3% of patients responded negatively compared to 32% of caregivers. Both groups were only minimally interested in future invasive ventilation.

Author conclusions:
Factors contributing to quality of life, depression, and attitudes toward treatment options need to be periodically explored with patients and caregivers throughout the course of the illness. Health care professionals should recognize that the needs and goals of the two groups might differ.</td>
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<td>Umpleby 2015
Journal paper / <u>conference abstract</u></td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr></table></td>
<td>Data relating to NIV provision and usage:</td>
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Country: UK
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<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Review of case notes</td></tr>
</table>
Aim of study: To describe a joint palliative/respiratory clinic
Data collection method:
Sample size: 23
Identification/recruitment: N/A
</td>
<td>
Measures
<table>
<tr><td>Descriptive</td></tr>
</table>
<table>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>18 limb, 3 bulbar, 2 respiratory</td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>Not reported</td></tr>
</table>
</td>
<td>
All patients commenced on NIV had end of life discussions.
16 had lung function tests performed.

Author conclusions:
A MDT approach involving respiratory medicine, palliative care and community physiotherapy ensures MND sufferers can discuss NIV and end of life care.
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<td>
Vandenberghe 2013
<u>Journal paper</u> / conference abstract
Country: France
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up: 34 months</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>
Aim of study: To explore factors affecting tolerance of NIV
Data collection method:
</td>
<td>
Participant characteristics:
Measures
<table>
<tr><td>Tolerance</td></tr>
</table>
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td></td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td>55 were tolerant, 18 poorly tolerant</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>Quarterly monitoring
Most were prescribed NIV by bi-level positive airway pressure in the S/T mode. A few subjects were treated</td></tr>
</table>
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<td>
Data relating to NIV provision and usage:
NIV was proposed when at least one clinical respiratory symptom was present (orthopnea of under 3 months onset; dyssomnia due to respiratory sleep disorders, with insomnia or suffocating wake-ups; nightmares; headaches;non-restorative sleep; paradoxical breathing), in association with at least one abnormal pulmonary function value (eg slow vital capacity <50% of predicted; nocturnal SpO2 of <90% for >5% of recording time).
Tolerance after the first day of use predicted tolerance at one month.
3 factors predicted good NIV
</td>
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</table>

Sample size: **Identification/recruitment:**	with the volume-targeted NIV method, following immediate intolerance to the bi-level positive airway pressure mode after a 4-hour trial. Any pooling of saliva was treated either by suction, medical treatment, botulinum toxin, or by a combination of all 3 before NIV initiation. Subjects were discharged from hospital on average after 2–3 days. When subjects went home, home visits were performed systematically: the day of going home, at 15 days, and at 48 hours before the evaluation at 1 month, by the nurse and home technician who delivered material. The interface of 2 subjects was changed from a nasal mask to an oronasal commercially available model. No subjects changed from pressure-targeted to volume-targeted NIV, or vice versa.		tolerance (more than 4 hours usage per night): absence of airway secretions accumulation prior to NIV onset (odds ratio 11.5); normal bulbar function at initiation of NIV (odds ratio 8.5); and older age (weakly significant, odds ratio 1.1). Among the poorly tolerant subjects, 18/73 had airway secretion accumulation: among the tolerant subjects, 55/73 had airway secretion accumulation. There were statistical differences between the 2 groups at NIV onset, with a lower rate of paradoxical breathing (P =0.03) and a lower rate of airway secretion accumulation (P =0.05) in the tolerant group than in the poorly tolerant group. **Author conclusions**: The most important and significant predictive factors were absence of airway secretion accumulation prior to starting NIV, and having non-bulbar ALS rather than bulbar ALS at initiation. The association between older age and NIV tolerance was weakly significant. Bulbar patients need intensive and prolonged monitoring at NIV onset to maximize its compliance. Poor tolerance and intolerance to NIV can perhaps be reduced for some additional ALS patients by controlling airway secretion

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<td></td>
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<td>accumulation by mechanically assisted cough.</td>
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<tr>
<td>Veldhuis 2015
<u>Journal paper</u> / conference abstract
Country: Netherlands
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr><tr><td>Other (specify)</td><td>Case study</td></tr></table>Aim of study: To explore the use of a chin lift
Data collection method: Unclear
Sample size: 1
Identification/recruitment: Unclear</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td></td></tr><tr><td>Sex</td><td>Female</td></tr><tr><td>Age</td><td>60</td></tr><tr><td>NIV usage</td><td></td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
Descriptive

Details of technology/NIV
A mandibular advancement device was fabricated.</td>
<td>Data relating to NIV provision and usage:

With a combination of a MAD and NIV, the upper airway obstructions were overcome and a good ventilation and adherence to therapy were seen.

Author conclusions:
When there is the presumption of airway obstructions in combination with an ineffective NIV, we advise to perform a chin lift to assess whether the obstructions can be overcome by a more anterior jaw position. If that is the case, NIV may be combined with MAD to establish effective ventilation and avoid the use of TV.</td>
</tr>
<tr>
<td>Vitacca 2013
<u>Journal paper</u> / conference abstract
Country: Italy
<table><tr><td>RCT</td><td></td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td>X</td></tr><tr><td>Other (specify)</td><td></td></tr></table></td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Pneumonology units</td></tr><tr><td>Condition</td><td>ALS and other neuromuscular conditions</td></tr><tr><td>Onset</td><td>N/A</td></tr><tr><td>Sex</td><td>N/A</td></tr><tr><td>Age</td><td>N/A</td></tr><tr><td>NIV usage</td><td>N/A</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
Survey responses

Details of technology/NIV</td>
<td>Data relating to NIV provision and usage:
The proportion of responding pneumology units that reported that they assess respiratory function at the first referral was near 100%, slow sitting vital capacity (VC) and arterial blood gases (ABGs) were routinely measured, whereas nocturnal oximetry, maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), and maximum sniff nasal pressure were less frequently evaluated.
Nocturnal oximetry,</td>
</tr>
</table>

Aim of study: To explore current practice **Data collection method:** Survey **Sample size:** 76 units **Identification/recruitment:** Identified by a registry	Not provided		cardiorespiratory monitoring, and polysomnography were considered necessary only if the patient was symptomatic. Overall, 70% of pneumology units used nocturnal respiratory studies to assess sleep-disordered breathing during follow-up. Frequency of follow-up visits was individualized in most centres, according to disease stage and the patient's need, rather than at fixed time intervals. Daytime hypercapnia, sleep-related hypoxemia, and a VC of 50% of predicted were the parameters most commonly followed to initiate NIV. The symptoms most likely to trigger NIV prescription were dyspnea on exertion, fatigue, and orthopnea. A multidisciplinary team approach to care of patients with ALS was employed in approximately 90% of pneumology units All units provided a structured training program, including family and caregiver education. High referring centres assessed respiratory muscle function and cough ability more accurately and were more likely to consider intervention with NIV when respiratory muscles strength was reduced. **Author conclusions**: Combined pulmonary function evaluation, long-term NIV, and

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<td>assisted coughing techniques have become the usual care for ALS individuals in Italy. Provision of information on respiratory complications and end-of-life decisions is still insufficient and needs to be improved, so patients and caregivers can be more active participants in disease management.</td>
</tr>
<tr>
<td>Volanti 2009
Journal paper / <u>conference abstract</u>
Country: Italy
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cohort</td></tr>
</table>
Aim of study: To explore factors associated with tolerance
Data collection method: Clinical testing
Sample size: 115
Identification/recruitment: Unclear</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>38 severe bulbar, 65 mild/moderate impairment</td></tr>
<tr><td>Sex</td><td>75 male 40 female</td></tr>
<tr><td>Age</td><td></td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
Survival
Tolerance

Details of technology/NIV
Not reported</td>
<td>Data relating to NIV provision and usage:
As expected, the majority of the intolerant patients had mild/moderate (47.3%) or severe (43.63%) bulbar impairment at NIV initiation.
Among the group with severe bulbar impairment, patients who tolerated NIV survived longer than those who were intolerant (P < 0.001). Further, we found that the bulbar patients tolerant to NIV come to the ALS Clinic more often than those intolerant after NIV indication (P = 0.0001).

Author conclusions:
This study shows that a regular follow-up in a multidisciplinary ALS Clinic after NIV indication could increase tolerance to NIV and survival, even in patients with severe bulbar impairment.</td>
</tr>
<tr>
<td>Volanti 2011</td>
<td>Participant characteristics:</td>
<td>Data relating to NIV provision</td>
</tr>
</table>

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<td>

<u>Journal paper</u> / conference abstract
Country: Italy

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up:	
Mixed method	
Cross-sectional	
Other (specify)	Cohort

Aim of study: To explore predictors of compliance
Data collection method: Clinical tsting
Sample size:37
Identification/recruitment: Consecutive

</td>
<td>

Measures

Tolerance

Type of group	Patients
Condition	ALS
Onset	32 severe or mild-moderate bulbar impairment
Sex	
Age	
NIV usage	
Other (specify)	

Details of technology/NIV

Not reported

</td>
<td>

and usage:
The mean time interval for adaptation to ventilation was 5+/-2 days, but patients remained in hospital for an average extended period of one week. Thirty-five of the 37 patients who started non-invasive ventilation, including those with severe bulbar impairment, remained tolerant at twelve months.

Author conclusions:
An intensive educational training and adaptation on non-invasive ventilation, when performed in a hospital multidisciplinary setting, increases compliance and tolerance over time, even in those patients with severe bulbar impairment.

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Vrijsen 2016
<u>Journal paper</u> / conference abstract
Country: Belgium

RCT	
Non-RCT	
CBA	
BA	
Comparator:	
Length of follow up: One month	
Mixed method	
Cross-sectional	
Other (specify)	Cohort

Aim of study: To explore the effects

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<td>

Participant characteristics:

Measures

Type of group	Patients
Condition	ALS
Onset	18 bulbar
Sex	
Age	
NIV usage	
Other (specify)	

</td>
<td>

Data relating to NIV provision and usage:
Non-bulbar patients improved in sleep architecture and oxygen and carbon dioxide levels while bulbar patients only improved oxygen saturation. PVA remained present at discharge (non-bulbar 54 (21-101) and bulbar 31 (9-39)/h sleep) and one month (non-bulbar 31 (9-39) and bulbar 32 (17-55)/h sleep), with ineffective effort as most prominent asynchrony.
Leaks also persisted after titration (non-bulbar 16.6 (3.1-44.6) and bulbar 5.1 (0.0-19.5)% of total sleep time (TST)) and one month (non-

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<td>of patient-ventilator asynchrony
Data collection method:
Sample size: 35
Identification/recruitment: Unclear</td>
<td>Full-video polysomnography, with incorporation of transcutaneous carbon dioxide and ventilator software, was used to analyse sleep epoch-by-epoch and respiratory events and PVA breath-by-breath.
Sleep, PVA and leaks were evaluated at discharge and after one month.

Details of technology/NIV
NIV was titrated during three consecutive nights.</td>
<td></td>
<td>bulbar 7.7 (1.4-29.3) and bulbar 12.7 (0.0-35.2)% TST
Author conclusions:
PVA and leaks have none to minor effect on sleep architecture. Although PVA and leaks remain present after meticulous NIV titration, these events seem not to interfere with sleep.</td>
</tr>
<tr>
<td>Vrijsen 2017
<u>Journal paper</u> / conference abstract
Country: Belgium
<table><tr><td>RCT</td><td>X</td></tr><tr><td>Non-RCT</td><td></td></tr><tr><td>CBA</td><td></td></tr><tr><td>BA</td><td></td></tr><tr><td colspan="2">Comparator:</td></tr><tr><td colspan="2">Length of follow up:</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Cross-sectional</td><td></td></tr><tr><td>Other (specify)</td><td></td></tr></table>Aim of study: To explore the effect of varying NIV modes
Data collection method: Clinical tests
Sample size:13
Identification/recruitment: Patients meeting criteria were included</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>6 bulbar</td></tr><tr><td>Sex</td><td>11 male</td></tr><tr><td>Age</td><td>Mean 57</td></tr><tr><td>NIV usage</td><td>None prior to study</td></tr><tr><td>Other (specify)</td><td></td></tr></table>Measures
Oxygen saturation
Sleep respiratory events

Details of technology/NIV
After a diagnostic polysomnography, NIV was titrated with a Trilogy 100 ventilator (Philips, Murrysville, PA,</td>
<td></td>
<td>Data relating to NIV provision and usage:
ST mode showed better results in gas exchange (minimal SpO2 %: 83 (80-89)% vs 87 (84-89)%; oxygen desaturation index: 15 (5-28)/h sleep vs 7 (3-9)/h sleep; PtcCO2 >55mm Hg: 20 (0-59)% vs 0 (0-27)% total sleep time for S and ST mode, respectively, all P<0.05) and respiratory events (obstructive: 8.9 (1.2-18.3)/h sleep vs 1.8 (0.3-4.9)/h sleep and central: 2.6 (0.4-14.1)/h sleep vs 0.2 (0.0-1.1)/h sleep for S and ST mode, respectively, both P<0.01).
No differences in sleep architecture were found.
Ineffective efforts and respiratory events were more frequently present in S mode. Nevertheless,</td>
</tr>
</table>

	USA) which incorporates Digital AutoTrak. In the afternoon, patients were titrated with pressure-cycled ventilation in S mode, starting with an inspiratory positive airway pressure (IPAP) of 8 cmH_2O and an expiratory positive airway pressure (EPAP) of 4 cmH_2O to get accustomed to NIV. During a nap (60–90 min) with polysomnography, IPAP was further titrated to reach a tidal volume of at least 6 mL/min/kg ideal body weight. IPAP could be further increased according to gas exchange measurements. In the presence of obstructive apnoeas, EPAP was titrated to resolve these events. The settings achieved during the afternoon nap were applied during the following night. NIV settings were further adjusted according to oxygen saturation (SpO_2%), $PtcCO_2$, respiratory events and PVA. IPAP and EPAP, as well as the interface were similar for the night on S and ST modes after randomization. The BURR was set at 1–2 breaths beneath the spontaneous breathing frequency measured during the non-rapid eye movement sleep of the diagnostic polysomnography.		four patients were discharged on S mode as these patients showed clinically better results for sleep architecture, gas exchange, arousal awakening and PVA during the night on S mode. These patients had a lower arterial carbon dioxide tension ($PaCO_2$) ($P = 0.08$) before the start of NIV, suggesting that these patients had less decrease in central respiratory drive or still had better inspiratory muscle strength. **Author conclusions**: ST mode shows better results in gas exchange, respiratory events and PVA. Nevertheless, accurate NIV titration remains necessary as some patients show equal or better results when using the S mode. Decisions on NIV mode should be made on an individual basis. Nocturnal monitoring plays a major role in this decision-making and should be performed during NIV titration procedures. Poly(somno)graphy to titrate NIV could provide important information on respiratory events, PVA and gas exchange.
Yamada 2001 **Journal paper / conference abstract** **Country:** Japan **RCT** ☐ **Non-RCT** ☐	**Participant characteristics:** **Type of group**: Patients **Condition**: ALS **Onset**: **Sex**:		**Data relating to NIV provision and usage:** BNPAP ventilation can be a cause of serious gastric insufflation in a patient who lies supine, especially

CBA		**Age**		after a meal due to the injection of inspiratory flow into the esophagus, aerophagia, and air trapping below the gastroesophageal junction. **Author conclusions**: Attention should be paid to avoiding this complication by having the patient sit up for about half an hour after a meal.
BA		**NIV usage**		
Comparator:		**Other (specify)**		
Length of follow up:				
Mixed method				
Cross-sectional				
Other (specify)	Case study			
Aim of study: To report a case study **Data collection method:** Description **Sample size:** 1 **Identification/recruitment:** Unclear		Measures Descriptive Details of technology/NIV Bilevel nasal positive airway pressure (BNPAP) ventilation (BiPAP; Respironics; Murrysville, PA).		
Yamauchi 2013 ab/2014 **Journal paper / conference abstract** **Country:** Japan		**Participant characteristics:**		**Data relating to NIV provision and usage:** Criteria for NIV when DCMAP decreased below 220 μV for group B and above for group A. Although respiratory function parameters were significantly worse in group B compared with group A at NIV initiation, more than 80% of the patients in both groups developed nocturnal desaturation during sleep. While phrenic nerve conduction study is useful for the evaluation of respiratory dysfunction in ALS, decreased SNIP and nocturnal desaturation were often observed in patients with respiratory insufficiency but preserved DCMAP. DCMAP may not be
RCT		**Type of group**	Patients	
Non-RCT		**Condition**	ALS	
CBA		**Onset**	50% bulbar involvement	
BA		**Sex**	22 female, 21 males	
Comparator: NIV initiated when DCMAP normal versus below normal limits		**Age**	Mean 62	
Length of follow up: 2 years		**NIV usage**		
Mixed method		**Other (specify)**		
Cross-sectional				
Other (specify)	Cohort			
Aim of study: To examine the correlation between respiratory insufficiency and diaphragmatic		Measures Respiratory function tests FVC, NPO, blood gas analysis Details of technology/NIV		

<table>
<tr>
<td>compound muscle action.
Data collection method: Clinical tests
Sample size: 17 + 26
Identification/recruitment: Unclear</td>
<td>DCMAPs were recorded using a Viking IV electromyograph (Nicolet Biomedical, Madison, USA). The phrenic nerve was stimulated transcutaneously with 0.2-ms rectangular pulses using a bipolar electrode, and pressure was applied to the cathode inferomedially at the supraclavicular fossa.</td>
<td>always a significant biomarker to determine the need for NIV. These results suggest the need for nocturnal pulsed oximetry to determine when to initiate NIV. SNIP should be recommended to monitor respiratory function and predict survival in patients with ALS.

Author conclusions:
Diaphragmatic compound muscle action potential (DCMAP) may not accurately indicate hypoventilation in some ALS cases. Respiratory impairment with preserved DCMAPs was seen in some ALS patients. The decision to initiate NIV in patients with ALS should be made based on symptoms of sleep disorder and nocturnal pulsed oximetry showing reduced oxygen tension during sleep.</td>
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<tr>
<td>**Andersen 2018/Kuzma-Kosakievicz 2016**
Journal paper / conference abstract
Country: Germany, Poland and Sweden
<table>
<tr><td>**RCT**</td><td></td></tr>
<tr><td>**Non-RCT**</td><td></td></tr>
<tr><td>**CBA**</td><td></td></tr>
<tr><td>**BA**</td><td></td></tr>
<tr><td colspan="2">**Comparator:**</td></tr>
<tr><td colspan="2">**Length of follow up:**</td></tr>
<tr><td>**Mixed method**</td><td>X</td></tr>
</table>
</td>
<td>**Participant characteristics:**
<table>
<tr><td>**Type of group**</td><td>Patients</td></tr>
<tr><td>**Condition**</td><td>ALS</td></tr>
<tr><td>**Onset**</td><td>Mean 37 months</td></tr>
<tr><td>**Sex**</td><td>131 male / 113 female</td></tr>
<tr><td>**Age**</td><td>Mean 61.35 years</td></tr>
<tr><td>**NIV usage**</td><td>Germany 35%; Poland 5%; Sweden 22%</td></tr>
<tr><td>**Other (specify)**</td><td>PEG: Germany 11%; Poland 6%; Sweden 23%</td></tr>
</table>
Measures
Views and perceptions</td>
<td>**Data relating to NIV provision and usage:**
Patients from Germany and Sweden were most likely to stop PEG, whilst Swedish patients were most likely to stop IV and NIV. Polish patients were least likely to stop any device ($p<0.001$). Preferences to terminate invasive devices in the future were not associated with physical function but were associated with duration of illness ($p<0.006$). Termination of non-invasive devices in the future was not associated with any clinical measure. Non-termination of devices was</td>
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<table>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To analyse decision making in therapeutic options for ALS within a socio-cultural context.
Data collection method: Structured interviews
Sample size: 244
Identification/recruitment: Consecutive ALS patients over two years who met inclusion criteria were invited (n=313). Lack of time, fatigue or inability were most cited reasons for not participating.
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Details of technology/NIV
<table><tr><td>N/R</td></tr></table>
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associated with religiousness and conservatism (p<0.002), whereas depression was associated with termination of devices (NIV p=0.23; IV p<0.008). QoL and financial support were not associated with decisions (p<0.05).
Author conclusions:
Patient decisions on future therapeutic care are related to cultural background.
</td>
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<td>
Bohm 2014
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td>X</td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Aim of study: To identify possible determinants of decision making process
Data collection method: Survey and interviews
Sample size: 100 / 10
Identification/recruitment: NR
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>NR</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>NR</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table><tr><td>Views and perceptions</td></tr></table>
Details of technology/NIV
<table><tr><td>N/R</td></tr></table>
</td>
<td>
Data relating to NIV provision and usage:
Family bonding was a strong determinant of decisions to prolong life. 93% of patients named the wishes of their caregivers as important for them.79% declared that the opinion of their caregivers influences their decisions. Increasing number of patient's children showed significant impact on the decisions to prolong life (p = 0.03, R2 = 0.38). Patients showed a strong need for autonomy, a strong determinant of decisions to shorten life (p = 0.04, R2 = 0.51). Degree of depression (p < 0.01, R2 = 0.21) and religiousness (p = 0.02, R2 = 0.23) had a significant influence on fatal decision making. Cognitive impairments however had no impact on decisions (all p > 0.05).
Author conclusions:
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<td>There is a discrepancy between the patients need for autonomy and the influence of the patient's family bonding on decisions. Patients that are more influenced by their need for autonomy decide towards life shortening treatments, whereas the patients that are influenced by their family ties tend to decide towards life prolonging treatments. Among other determinants, conflicting issues of subjective feeling of autonomy and family bonding have to be considered by the multidisciplinary teams in counselling, treatment and therapy of ALS patients.</td>
</tr>
<tr>
<td>Foley & Hynes 2018
Journal paper / conference abstract
Country: Ireland
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>Review</td></tr>
</table>
Aim of study: To examine patient/family relationship in decision making pertaining to care.
Data collection method: Review of peer reviewed research 2007-2017
Sample size: 47 studies (55 papers)
Identification/recruitment: Medical</td>
<td>Participant characteristics:
<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>N/A</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>Varied</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table>
<tr><td>Views and perceptions</td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>N/R</td></tr>
</table></td>
<td>Data relating to NIV provision and usage:
One German study showed that cognitive impairment / behavioural change (as rated by caregiver) were not associated with use or withdrawal of ventilation.
A Japanese study identified the presence of a spouse was a significant factor when making a decision to undergo IV. Another Japanese study found disparity, with family caregivers more in favour of IV than patients.
In the UK, one study reported good palliative care outcomes (rated by family caregivers) were associated with patient refusal of NIV, and that lower caregiver strain and higher wellbeing was associated with patient intervention refusal.
Also in the UK, three papers reported</td>
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<td>and nursing database searches.</td>
<td></td>
<td>physical and psychological challenges for patients and their family caregivers when using ventilation, though they engaged with it because of the benefits to both patients and caregivers. Another UK study reported that family enabled patients to share the burden of decision making about interventions. Other qualitative studies showed that family caregivers took on the burden of care associated with ventilation because of the positive effects for the patient.
One Danish study reported that a reason for patient wish to withdraw IV was a loss of meaning in life. Family caregivers I retrospect had been apprehensive about the looming end of life but had gone along with the patient’s wishes.
Family want more information about ventilation than do patient and for patients to plan for the future before patients are ready. Patients do not want to place a burden on family caregivers, who in turn want to be advocates for the patient.
Author conclusions:
Attention to family member roles beyond those of the primary caregiver are necessary in decision making.</td>
</tr>
<tr>
<td>Martin 2014
Journal paper / conference abstract
Country: UK
<table><tr><td>BA</td><td></td></tr><tr><td>CBA</td><td></td></tr></table></td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients and caregivers</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>≥ 6 months (mean</td></tr></table></td>
<td>Data relating to NIV provision and usage:
32 patients made at least one intervention decision (18 died without making a decision). 19 accepted and two refused NIV. Of those that died</td>
</tr>
</table>

Comparator: **Cross-sectional** | **Length of follow up:** **Mixed method** | X **Non-RCT** | **Other (specify)** | X cohort **RCT** | **Qualitative** | **Other (specify)** | **Aim of study:** To identify factors associated with acceptance of NIV. **Data collection method:** Baseline physical, cognitive, psychological and health service use measures. Interviews **Sample size:** 78 patients (from 178 invited and 81 consented); 50 caregivers **Identification/recruitment**: South East ALS register (SEALS). At study enrolment, none had made a clinical decision about NIV.		Measures Views and perceptions Details of technology/NIV N/R	7.8 / 12.5 months (abstract), max 60 months) **Sex** | 49 males; 29 females **Age** | Mean 62.5 (±11.8) **NIV usage** | Not yet referred **Other (specify)** | 20.5% indicated awareness of NIV, but were reluctant to think about it in advance	following a decision, NIV was decided on close to end of life (mean 2.7 months). Being more unwell at baseline (low BMI, poorer speech / swallowing) and poorer prognosis was predictive of decision making, whether for NIV or gastrostomy. Also associated with decisions were higher IQ, longer time in education and "active" approach (actively seeking information), to the two interventions. Post-decision assessment showed that being employed, understanding the illness well, having an active approach to intervention and low depression score was associated with likelihood for refusal of intervention. Being more religious was associated with refusal at baseline and post-decision. For carers, higher wellbeing and lower caregiver strain was associated with patient refusal of interventions. Better palliative outcome rating at baseline was most associated with patient refusal, though by post-decision this changed, possibly due to poorer outcomes based on refusal. **Author conclusions:** The results provide a framework for understanding complex factors that need to be taken into account when discussing intervention with ALS patients.
Palmer 2011 Journal paper / conference abstract **Country:** UK **RCT** |	**Participant characteristics:** **Type of group** | Patients **Condition** | MND			**Data relating to NIV provision and usage:** 71% of patients were eventually concordant, 19% did not tolerate NIV

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<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td></td></tr>
<tr><td>Other (specify)</td><td>X</td></tr>
</table>

Aim of study: Concordance of patients with NIV intervention
Data collection method:
Retrospective case note review April 2004 – March 2011
Sample size: 42
Identification/recruitment: NR
</td>
<td>
<table>
<tr><td>Onset</td><td>Mean 13.9 months</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>Yes</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table>
<tr><td>Views and perceptions</td></tr>
</table>
Details of technology/NIV
<table>
<tr><td>N/R</td></tr>
</table>
</td>
<td>and 10% died. Concordance was greater and more rapid in hospital than at home (76% vs 69%; 4.4 days vs 14.2 days respectively). NIV was tolerated well in those with symptomatic and physiological requirement (84%). 75% failure rate in physiological requirement only; 80% concordance in symptom requirement only. Most common symptom was daytime sleepiness (81%). Mean survival from initiation was 10.2 months (range 0.67-84). Three patients moved from NIV to IV, one of whom survived a further 5 years.
Author conclusions:
There is a tendency for MND patients to be more concordant with NIV that is started in hospital than at home, and initiation is more rapid. Patients without symptoms are less tolerant of NIV.</td>
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<td>
Rowe-Haynes et al 2012 (linked to Faull, Oliver and Phelps)
Journal paper / <u>conference abstract</u>
Country: UK
<table>
<tr><td>RCT</td><td></td></tr>
<tr><td>Non-RCT</td><td></td></tr>
<tr><td>CBA</td><td></td></tr>
<tr><td>BA</td><td></td></tr>
<tr><td colspan="2">Comparator:</td></tr>
<tr><td colspan="2">Length of follow up:</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Cross-sectional</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>
Participant characteristics:
<table>
<tr><td>Type of group</td><td>Members of the Association of Palliative Medicine (60% directly involved in NIV withdrawal)</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>NR</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>Withdrawal</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
Measures
<table>
<tr><td>Views and perceptions</td></tr>
</table>
Details of technology/NIV
</td>
<td>Data relating to NIV provision and usage:
5% used a protocol or guideline. Most found the process of NIV withdrawal practically, emotionally and ethically challenging. Of those who found it very challenging, 70% reported practically challenging, 75% emotionally challenging and 60% ethically challenging.
12% found NIV very emotionally challenging. Some common difficulties included lack of guidance on practical aspects of withdrawal, poor advance care planning and the need to support all involved to</td>
</tr>
</table>

Aim of study: To identify issues and challenges doctors have encountered when withdrawing NIV in MND patients. **Data collection method:** Survey **Sample size:** 134 **Identification/ recruitment:** Electronic questionnaire	N/R	prevent conflict. Statements relating to the emotional burden were diverse but suggest a significant personal impact is felt by many palliative care doctors. **Author conclusions:** Withdrawal of NIV in patients with MND appears to pose multiple challenges to palliative care doctors. Development of guidelines and a clear ethical statement of conduct may help with some of the practical and ethical challenges. Emotional issues appear more complex. Further research into the challenges faced by all professionals in the withdrawal of NIV is necessary.

MND Review Qualitative study data extractions

<table>
<tr>
<td>Andersen 2018 (linked to Kuzma-Kosakievicz 2016)

Journal paper / conference abstract

Country: Germany, Poland and Sweden

<table>
<tr><td>Qualitative</td><td></td></tr>
<tr><td>Mixed method</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To analyse decision making in therapeutic options for ALS within a socio-cultural context.

Data collection method: Face-to-face interviews</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>Mean 37 months</td></tr>
<tr><td>Sex</td><td>131 male / 113 female</td></tr>
<tr><td>Age</td><td>Mean 61.35 years</td></tr>
<tr><td>NIV usage</td><td>Germany 35%; Poland 5%; Sweden 22%</td></tr>
<tr><td>Other (specify)</td><td>PEG: Germany 11%; Poland 6%; Sweden 23%</td></tr>
</table>
</td>
<td>Author identified themes

Data relating to NIV provision and usage:

Patients from Germany and Sweden were most likely to PEG, whilst Swedish patients were most likely to stop IV and NIV. Polish patients were least likely to stop any device (p<0.001). Preferences to terminate invasive devices in the future were mot associated with physical function but were associated with duration of illness (p<0.006). Termination of non-invasive devices in the future was not associated with any clinical measure.
Non-termination of devices was associated with religiousness and conservatism (p<0.002),</td>
</tr>
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<table>
<tr>
<td>Theoretical underpinning: N/R

Sample size: 244

Identification/recruitment:

Consecutive ALS patients over two years who met inclusion criteria were invited (n=313). Lack of time, fatigue or inability were most cited reasons for not participating.</td>
<td></td>
<td>whereas depression was associated with termination of devices (NIV p=0.23; IV p<0.008). QoL and financial support were not associated with decisions (p<0.05).

Author conclusions:

Patient decisions on future therapeutic care are related to cultural background.</td>
</tr>
<tr>
<td>Ando 2010 / Piggin 2009

Journal paper / conference abstract

Country: UK

<table>
<tr><td>Qualitative</td><td>X</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To determine psychological issues important in patients declining or failing to tolerate NIV, particularly those issues which contribute to treatment failure.

Data collection method: Interviews

Theoretical underpinning: Not reported

Sample size: 11 patients who did not tolerate NIV (10 interviews)

Identification/recruitment: Not reported</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>8 limb
3 bulbar</td></tr>
<tr><td>Sex</td><td>8 male
3 female</td></tr>
<tr><td>Age</td><td>Mean 74.1 years</td></tr>
<tr><td>NIV usage</td><td>Intolerant</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes

Personal perceptions of NIV consequence,
Maintenance of self-identity,
Negotiation of the disease symptoms
External influences

Data relating to NIV provision and usage (Piggin 2009):

Pre-NIV, framing in regard to disease progression; for some, NIV represented a negative "milestone" in physical decline, whilst for others, an opportunity/hope for improvement.

Most reluctant to consider "realities" of NIV until use was imminent. Resignation and anxiety common themes. Resistance increased where the link between ventilation and actual symptoms was poorly understood, creating conflict between subjective/objective need for treatment.

Most patients perceived no subjective need for NIV describing decision making as led by professionals and family members (having "no choice"). After ventilation many reported that the non-invasive nature of NIV provided choice - reassuring and empowering.</td>
</tr>
</table>

		Post-NIV, improved sleep/energy levels; negative aspects outweighed by positive physical effects. Managing expectation important; a minority finding effects disappointing or the struggle to adjust to the machine actually increasing sleep disturbance and anxiety. Patients reporting no effect still motivated to continue "just in case" fearing no change with NIV might equate to significant physical decline without NIV. **Author conclusions:** Diversity of experience and feeling – dynamically shifting physical and emotional landscape. Before treatment NIV perceived with alarm / marker of decline, then positive as beneficial treatment. Some expectations were unrealistic leading to disappointment. Ambivalence before NIV changed when sleep and energy levels improved post-NIV. This work suggests managing expectations is a central issue in using NIV in MND. **Data relating to NIV provision and usage (Aldo 2010):** 17 established on NIV; 11 declined or failed to tolerate NIV. Perceived negative outcomes of NIV were linked to self-identity which became vulnerable following MND and physical deterioration. Self-identity was further impacted by NIV. There were discrepancies between HCP recommendations and patient's perceived need.

<table>
<tr>
<td></td>
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<td>Author conclusions:

Understanding the implications of NIV for individuals is important if treatment is to be offered optimally and sensitively.</td>
</tr>
<tr>
<td>Ando 2014

<u>Journal paper</u> / conference abstract

Country: UK

<table>
<tr><td>Qualitative</td><td>X</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To understand why patients decline/withdraw from NIV

Data collection method: Semi-structured interviews. Five interviews pre NIV and seven interviews post NIV trial.

Theoretical underpinning: Phenomenology

Sample size: 9

Identification/recruitment: From a cohort of 35 patients offered NIV, these patients were those that had declined/withdrawn NIV. Identified at time of referral for respiratory assessment.</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>Confirmed diagnosis of MND (El Escorial criteria), no cognitive or behavioural dysfunction</td></tr>
<tr><td>Onset</td><td>6 limb, 3 bulbar. 6 bulbar symptoms at time of study</td></tr>
<tr><td>Sex</td><td>7 male, 2 female</td></tr>
<tr><td>Age</td><td>Mean age 67</td></tr>
<tr><td>NIV usage</td><td>6 withdrew from NIV, 1 used for 2 months before withdrawal, 2 did not use</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes: preservation of the self, negative perceptions of NIV, negative experience with health care services, and not needing NIV.

Data relating to NIV provision and usage:

Experience of healthcare - Two patients reported receiving poor service from the hospital, and this appeared to influence their decision not to even consider a trial of NIV. One described appointments “not being an enjoyable experience”, the other reported multiple cancellations of appointments which was perceived as disappointing, and being a “rejection of his needs”. One patient expressed wish to avoid all hospitals. The study authors described this as a wish to be left alone for the limited time he had left.

Role of professionals – One patient described staff being overly forceful and infringing his autonomy by trying to change his mind about NIV and attending appointments.

Timing - Seven participants were unsure of the need for NIV, with them perceiving limited difficulties with their breathing, even when presented with test results.

One patient who used NIV successfully withdrew when his condition deteriorated.

Control - NIV could be perceived as a threat to</td>
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<td></td>
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<td>the self, at a time when the illness was causing loss of control. Interactions with healthcare staff could be seen as further disempowerment, with rejection of NIV an attempt to preserve identity and independence.

Author conclusions: A sensitive holistic evaluation of NIV decline/withdrawal should be made, to understand the psychological aspects underpinning decision-making in particular related to the sense of self.</td>
</tr>
<tr>
<td><u>Ando 2014</u> / Abstracts Ando 2011a/ Ando 2011b /Ando 2012

<u>Journal paper</u> / <u>conference abstract</u>

Country: UK

<table>
<tr><td>Qualitative</td><td>X</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To explore patient perceptions of NIV treatment over time and how this affects adherence.

Data collection method: Multiple interviews

Theoretical underpinning:

Sample size: 5

Identification/recruitment: Invitation to participate at the stage of referral.</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>Median 29 months (Range 23-237)</td></tr>
<tr><td>Sex</td><td>4 male; 1 female</td></tr>
<tr><td>Age</td><td>Mean 59 years (range 51-75)</td></tr>
<tr><td>NIV usage</td><td>Mean 13 months (Range 12-14)
Mean 9 hours 27 minutes per day</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes

Experiences of NIV
Influence on attitudes
Perceived impact of NIV on prognosis

Data relating to NIV provision and usage:

Positive: Physical (sleep, tiredness, energy levels, SOB, oxygen levels, daily activity) and linked psychological (feeling more comfortable, being able to enjoy life) benefits of NIV discussed. Negative: Uncomfortable mask, strap and air pressure. These were not reported to trigger negative psychological affects but were accepted as part of treatment. The most common negative psychological effect was dependence.

Link between coping style and pattern of use. Resistance to MND did not necessarily follow through to resistance of NIV. Indeed, NIV was used to ensure continuation of social activities. Conversely, giving in to NIV could also mean giving in to MND. For 4 participants, an active coping style was linked to positive psychological benefits.</td>
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<td>The essentiality of NIV was linked to the fear of death. Two participants were reluctant to cling on to life and this followed through with reluctance to use NIV. Adaptive response to NIV was observed where perceived benefits outweighed concerns over prognosis.

Author conclusions:

Individual experience of NIV is based on interpretation of the illness and its perceived impact on the future, which in turn is affected by coping styles and attitude to life. However, hopelessness was found to be modifiable through use of NIV.

It is suggested that clinicians address patient representations of the disease where adherence to NIV is poor, and psychological intervention be considered. However, ultimately, patient wellbeing is more important than adherence.</td>
</tr>
<tr>
<td>Ashcroft 2016
Journal paper / <u>conference abstract</u>
Country: UK
<table><tr><td>Qualitative</td><td>X</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Other (specify)</td><td></td></tr></table>
Aim of study: To understand experiences of tele-monitoring in ventilated MND patients
Data collection method: Semi-structured interviews
Theoretical underpinning: N/R
Sample size: 7
Identification/recruitment: N/R</td>
<td>Participant characteristics:
<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>Median 14 months</td></tr><tr><td>Sex</td><td>5 male; 2 female</td></tr><tr><td>Age</td><td>Mean 63 years</td></tr><tr><td>NIV usage</td><td>Median 12 months</td></tr><tr><td>Other (specify)</td><td>6 months use of tele-monitoring device</td></tr></table></td>
<td>Author identified themes:
Technical challenges
Increased self-awareness
Taking initiative
Benefits of timely intervention
Reducing the unnecessary

Data relating to NIV provision and usage:
Tele-monitoring allowed patients to raise concerns or requests with HCPs, which enabled timely intervention. Use could also reduce time and cost of hospital appointments.
Author conclusions:
Tele-monitoring allowed patients to be actively involved in their care. Interventions were delivered in a timely way. Potential for routine use as a contact point.</td>
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<tr>
<td><u>Baxter 2013</u> / Abstract Baxter 2012a

<u>Journal paper</u> / <u>conference abstract</u>

“The initiation of non-invasive ventilation for patients with motor neuron disease: Patient and carer perceptions of obstacles and outcomes”

Country: UK

<table>
<tr><td>Qualitative</td><td>X</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To explore experiences of patients with MND and carers following recommendation to use NIV.

Data collection method: Interviews

Theoretical underpinning: N/R

Sample size: 20 patients with 17 carers

Identification/recruitment: Consecutive MND patients who met inclusion criteria were invited to participate.</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>15 male; 5 female</td></tr>
<tr><td>Age</td><td>≥60 years</td></tr>
<tr><td>NIV usage</td><td>Mean 0-10.5 hours per day
13 “regular” (mean 7.4 hours)</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes:

Potential barriers
Perseverance
Perceived Benefits

Data relating to NIV provision and usage:
Potential barriers:
Negative first impression.
Relief that device is compact and discreet.
Lack of confidence; may cause device to malfunction.
Preference for telephone / in- person support over written.
Negative sensation of air pressure.
Sleep disturbance (patient and carer).
Relatively easy to set up but more often used with carer support.
Dry mouth.
Leakage from mask.
Claustrophobic.
Perseverance:
Need to keep trying
Getting used to the device
Perceived Benefits
Improved sleep.
Greater energy / alertness
Improved daytime breathing
Better able to communicate
Impact of benefits for carers

Author conclusions:
Key recommendations for practice are in-person support, pre-empting potential difficulties, optimisation of secretion management before NIV; importance of discussion benefits with patients.</td>
</tr>
<tr>
<td><u>Baxter 2013</u> / Abstracts Baxter 2012b / Baxter</td>
<td>Participant characteristics:</td>
<td>Author identified themes</td>
</tr>
</table>

2012c

Journal paper / conference abstract

"The use of non-invasive ventilation at end of life in patients with motor neurone disease: A qualitative exploration of family carer and health professional experiences"

Country: UK

Qualitative	X
Mixed method	
Other (specify)	

Aim of study: To describe experiences of patients and carers of end-of-life care for MND using NIV.

Data collection method: Interviews

Theoretical underpinning:

Sample size: 24 (9 carers, 15 professionals) reporting on 10 patients following their death.

Identification/recruitment: Carers of consecutive MND patients who had decided to try NIV and met inclusion criteria were invited to participate. Professionals were identified by carers.

Type of group	Patients
Condition	MND
Onset	NR
Sex	NR
Age	60+ (patients)
NIV usage	Yes
Other (specify)	Carers: 6 wives, 3 husbands and one daughter.

Unexpected speed of deterioration
Hospitalisation vs dying at home
Attempts to resuscitate
Decision making regarding withdrawal of NIV
Peaceful final moments
Turning off the machine
Professional uncertainty regarding use of NIV
Positive impacts of NIV use
Concerns regarding NIV use

Data relating to NIV provision and usage:
Initiation of NIV provided a way for HCPs to broach the subject of patient wishes for the future.

Five patients were receiving 24hr NIV at the time of death. One stopped during the final month due to difficulties fitting the mask when physical function declined. One patient who used NIV at night died whilst not using NIV (during the day) and another three low users died without NIV use. No difficult decisions were made by these users.

Patients who had been using 24hr NIV wished to keep it in place to the end.

Descriptions of final hours differed little for NIV users and non-users (i.e. peaceful, no choking or struggling to breathe).

Here was an issue of whether the NIV was still breathing for the patient following what appeared to be death. HCPs reported telling carers that this was not the case; the patient triggers the machine to work.

Decisions were mainly supported by community teams rather than medical staff. HCPs reported fears about how stopping use of NIV would affect the end of life. Some weaned patients off by

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<td>turning the machine down or administering Midazolam to prevent awareness that the machine was being turned down.

HCPs reported the perception that NIV is like a ventilator and turning it off will kill the patient.

Carers of regular users perceived that NIV had extended life, whereas carers of low users who discontinued NIV did not report such benefits and felt NIV was an obstacle. HCPs reported NIV as comfort and reassurance in a similar way to oxygen therapy.

Majority of participants were positive about NIV. Three HCPs expressed concern that the mask impeded communication because it was noisy, and / or that patients could become dependent on the mask, which impeded mouth care at end of life.

Author conclusions:

NIV does not have a detrimental impact on end of life in MND patients and could be beneficial. Wishes regarding use vary at end stage and carers need to be clear about how NIV works.</td>
</tr>
<tr>
<td>Bohm 2014

Journal paper / <u>conference abstract</u>

Country: UK

<table>
<tr><td>Qualitative</td><td></td></tr>
<tr><td>Mixed method</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To identify possible determinants</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>NR</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>NR</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes

Data relating to NIV provision and usage:

Family bonding was a strong determinant of decisions to prolong life. 93% of patients named the wishes of their caregivers as important for them.79% declared that the opinion of their caregivers influences their decisions.

Increasing number of patient’s children showed significant impact on the decisions to prolong life</td>
</tr>
</table>

<table>
<tr>
<td>of decision making process

Data collection method: Survey and interviews

Theoretical underpinning:

Sample size: 100 / 10

Identification/recruitment: NR</td>
<td></td>
<td>(p = 0.03, R2 = 0.38). Patients showed a strong need for autonomy, a strong determinant of decisions to shorten life (p = 0.04, R2 = 0.51). Degree of depression (p < 0.01, R2 = 0.21) and religiousness (p = 0.02, R2 = 0.23) had a significant influence on fatal decision making. Cognitive impairments however had no impact on decisions (all p > 0.05).

Author conclusions:

There is a discrepancy between the patients need for autonomy and the influence of the patient's family bonding on decisions. Patients that are more influenced by their need for autonomy decide towards life shortening treatments, whereas the patients that are influenced by their family ties tend to decide towards life prolonging treatments. Among other determinants, conflicting issues of subjective feeling of autonomy and family bonding have to be considered by the multidisciplinary teams in counselling, treatment and therapy of ALS patients.</td>
</tr>
<tr>
<td>Faull 2014

Journal paper / conference abstract

Country: UK
<table><tr><td>Qualitative</td><td></td></tr><tr><td>Mixed method</td><td>X</td></tr><tr><td>Other (specify)</td><td></td></tr></table>
Aim of study: To identify issues (practical, emotional and ethical) and challenges for medical staff in regard to withdrawing NIV in MND.

Data collection method: Survey</td>
<td>Participant characteristics:

<table><tr><td>Type of group</td><td>Medical staff involved in caring for MND patients.</td></tr><tr><td>Condition</td><td>MND</td></tr><tr><td>Onset</td><td>N/A</td></tr><tr><td>Sex</td><td>N/A</td></tr><tr><td>Age</td><td>NR</td></tr><tr><td>NIV usage</td><td>Yes</td></tr><tr><td>Other (specify)</td><td></td></tr></table></td>
<td>Author identified themes

Data relating to NIV provision and usage:

58.5% doctors had been directly involved in withdrawing NIV. Those who had not been directly involved reported withdrawal of NIV as more of a challenge to them (scoring 7+) on all three dimensions, with one exception.

Over half of respondents scored 7+ on emotional scale with 20% scoring 9-10 out of 10.

Concerns:
Lack of guidelines
Whether or not to wean off NIV</td>
</tr>
</table>

<table>
<tr>
<td>Theoretical underpinning: NR

Sample size: 130

Identification/recruitment: Through Survey Monkey. Survey distributed to all members of the Association of Palliative Medicine of Great Britain and Ireland (APM) (n=993).</td>
<td></td>
<td>How to manage distressing symptoms
Use of sedative drugs (which and how)
Who should remove the mask
Time and planning burden
Communication difficulties (timing, sensitivity and limitations).
Large MDT involved in decision making process (time, and can lead to conflict) even where apparently clear ADRT
Timing and appropriateness of withdrawal
Clear intentions
Potential criticism – may be seen as euthanasia
Managing emotions of others
Causing harm or distress to patient
Death being related to an action (though acknowledged not the intention)
Author conclusions:

Doctors who had not been involved in NIV withdrawal were most likely to report challenges, suggesting that experience may mediate the perception of challenge. However, challenges continue with experience. Leadership is challenged by the scarcity of the event and lack of guidelines as well as emotional challenges.

Patients may wish for NIV to stop, but physical constraints mean the HCP team may have to carry out the wish. Long discussions with family and MDT are also effort and time consuming.

Challenges may be addressed partly by clear published guidelines, a clear ethical statement and mentorship for team members.</td>
</tr>
<tr>
<td>Faull 2014 (linked to Oliver and Phelps)

Journal paper / <u>conference abstract</u></td>
<td>Participant characteristics:

<table><tr><td>Type of group</td><td>Doctors (palliative, neurology, and</td></tr></table></td>
<td>Author identified themes</td>
</tr>
</table>

Country: UK

Qualitative	X
Mixed method	
Other (specify)	

Aim of study: To discover challenges to practice, identify perceptions of the best experience for patients and families and understand how involvement in withdrawing NIV can affect doctors.

Data collection method: Interviews

Theoretical underpinning: Not reported

Sample size: 18

Identification/recruitment: NR

	respiratory specialists and GPs)
Condition	MND
Onset	N/A
Sex	N/A
Age	N/A
NIV usage	Withdrawal
Other (specify)	

Data relating to NIV provision and usage:

Cases of withdrawal few but memorable, with tensions and emotions carried with them. Few had opportunity to share experiences with colleagues.

Clarity of ethical concerns and clinical decision making contrasts with complexity of wanting to carry out patient's wishes.

Medical indemnity organisations not clear about legal and professional acceptability of this or the stress of the situation.

Some doctors shared these viewpoints.

Author conclusions:

Withdrawal of NIV is a lonely and uncomfortable experience for doctors. Absence of guidance was a strong feature. Need to build consensus amongst those involved in discussions as well as actual withdrawal of NIV.

Foley & Hynes 2018

Journal paper / conference abstract

Country: Ireland

Qualitative	
Mixed method	
Other (specify)	Review

Aim of study: To examine patient/family relationship in decision making pertaining to care.

Data collection method: Review of peer

Participant characteristics:

Type of group	Patients
Condition	ALS
Onset	N/A
Sex	NR
Age	NR
NIV usage	Varied
Other (specify)	

Author identified themes

Sourcing information about ALS
Life prolonging and life ending interventions
Advanced care planning
Genetic testing
Support seeking
Family reliance and responsibility

Data relating to NIV provision and usage:

One German study showed that cognitive impairment / behavioural change (as rated by caregiver) were not associated with use or withdrawal of ventilation.

reviewed research 2007-2017 **Theoretical underpinning:** NR **Sample size:** 47 studies (55 papers) **Identification/recruitment:** Medical and nursing database searches.		A Japanese study identified the presence of a spouse was a significant factor when making a decision to undergo IV. Another Japanese study found disparity, with family caregivers more in favour of IV than patients. In the UK, one study reported good palliative care outcomes (rated by family caregivers) were associated with patient refusal of NIV, and that lower caregiver strain and higher wellbeing was associated with patient intervention refusal. Also in the UK, three papers reported physical and psychological challenges for patients and their family caregivers when using ventilation, though they engaged with it because of the benefits to both patients and caregivers. Another UK study reported that family enabled patients to share the burden of decision making about interventions. Other qualitative studies showed that family caregivers took on the burden of care associated with ventilation because of the positive effects for the patient. One Danish study reported that a reason for patient wish to withdraw IV was a loss of meaning in life. Family caregivers I retrospect had been apprehensive about the looming end of life but had gone along with the patient's wishes. Family want more information about ventilation than do patient and for patients to plan for the future before patients are ready. Patients do not want to place a burden on family caregivers, who in turn want to be advocates for the patient. **Author conclusions:** Attention to family member roles beyond those of

<table>
<tr>
<td></td>
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<td>the primary caregiver are necessary in decision making.</td>
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<tr>
<td>Greenaway 2015 (linked to Martin)

<u>Journal paper</u> / conference abstract

Country: UK

<table>
<tr><td>Qualitative</td><td>X qualitative component of a larger study</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To identify factors associated with decision-making re NIV and gastrostomy

Data collection method: Semi-structured interviews either post-decision to decline or post trial of NIV

Theoretical underpinning: None specified

Sample size: 21

Identification/recruitment: Recruited from register, part of a larger study of 78 patients. Referral for NIV and/or gastrostomy,</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>Confirmed diagnosis of ALS, duration of disease between 6 and 60 months;</td></tr>
<tr><td>Onset</td><td>Not reported</td></tr>
<tr><td>Sex</td><td>13 male, 8 female</td></tr>
<tr><td>Age</td><td>Range 41-76 years</td></tr>
<tr><td>NIV usage</td><td>All five offered it had accepted NIV.</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes: Patient-centric factors (perceptions of control, acceptance and need, and aspects of fear); external factors (roles played by healthcare professionals, family, and information provision); and the concept of time (including living in the moment and the notion of ‘right thing, right time’). These factors were inter-related.

Data relating to NIV provision and usage:

Choice - Wish to make active choices and have responsibility for lives, remaining in active control of their own body. Some participants focused on the present, rather than making choices regarding the future.

Role of Professionals -Reports of professionals as being very supportive and caring, showing humanity and providing reassurance. Importance of having trust in the professional, some patients reported perceiving a lack of expertise on ALS. Reports of feeling pressured to have an intervention, tension around who had control. The relationship between patient and professionals was important with support, or lack of support having an impact on decision-making.

Family - Dual role of family – as either helpful support or adding to emotional pressure to have an intervention.

Information - Report of varying levels of provision of information, and a lack of accuracy in the information. Those who decided against an intervention were more likely to actively seek</td>
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<td></td>
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<td>answers to their questions. Individuals differed in their information requirements. Making the decision seemed to be easier for those who wished for and had access to different sources of information. Related study from same authors found more information did not lead to greater acceptance.

Timing – Difficult to know when time was right due to variation in disease progression. Patients tended to be focused on current position rather than the future. Professionals giving non-specific advice such as better sooner than later was perceived as unhelpful.

Author conclusions: Patient decision-making processes are complex, and approaches need to be individualised. Patient focus on the present rather than the future was at variance with professional emphasis on early intervention which could be perceived as undue pressure. Need for cyclical and greater patient-focused pattern of professional support and advice.</td>
</tr>
<tr>
<td>Kuzma-Kozakiewicz 2016 (linked to Andersen 2018)

Journal paper / conference abstract

Country: Germany, Sweden and Poland

<table>
<tr><td>Qualitative</td><td></td></tr>
<tr><td>Mixed method</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To define determinants of decision</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>NR</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>Preferences</td></tr>
<tr><td>Other (specify)</td><td>Country:
Germany (n=265)
Sweden (n=71)
Poland (n=65)</td></tr>
</table>
</td>
<td>Author identified themes

Patient wellbeing and NIV preferences were different between countries. Swedish patients most autonomous and Polish patients most conservative.

Data relating to NIV provision and usage:

NIV in Germany and PEG in Sweden most commonly used in addition to highest preference for usage and ideation to turn off the devices (all $p<0.05$).</td>
</tr>
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<td>making between Germany, Sweden and Poland with comparable legal but different cultural and religious backgrounds.

Data collection method: Interviews and scales: ALS-FRS, disease duration, QoL, ACSA and SEIQoL, depression (ADF12), religious background (Idler) and personal values (Schwartz Value Scale).

Theoretical underpinning: Not reported

Sample size: 401

Identification/recruitment: Not reported</td>
<td></td>
<td>Polish patients were mostly undecided about the usage of NIV, and least likely to show ideation to turn off these devices. Preferences for hypothetical ideation to terminate treatments in case of physical decline was determined by residency only (p<0.001). Religiousness was a predictor for decisions for NIV (p<0.05) and for preferences for hypothetical ideation to terminate treatments. Decision status on IV was determined by conservatism. The more advanced the medical condition the more likely they decided for NIV (p<0.01).

Author conclusions:

Preferences on therapeutic options are primarily determined by medical condition. However, various other factors such as cultural background have major impact on decision making in ALS in different European countries.</td>
</tr>
<tr>
<td>Lemoignan & Ells 2010

<u>Journal paper</u> / conference abstract

Country: Canada

<table>
<tr><td>Qualitative</td><td>X</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To understand the experience of decision making about assisted ventilation for ALS patients.

Data collection method: Semi-structured interviews

Theoretical underpinning: Phenomenology</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients and their caregivers</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>16-132 months</td></tr>
<tr><td>Sex</td><td>6 male; 3 female</td></tr>
<tr><td>Age</td><td>36-72</td></tr>
<tr><td>NIV usage</td><td>6 used NIV</td></tr>
<tr><td>Other (specify)</td><td>2 LTMV (1 with NIV)
2 used no ventilation</td></tr>
</table>
</td>
<td>Author identified themes

Meaning of the intervention
Importance of context
Importance of values
The effect of fears
The need for information
Adaptation / acceptance of intervention

Data relating to NIV provision and usage:
NIV was a means of relieving symptoms of respiratory failure, as “soothing”, in contrast to LTMV which was seen as “life or death”.
NIV was easy to use or stop using, non-invasive, not risky. LTMV was associated with being bed bound and unable to move or engage with people.</td>
</tr>
</table>

Sample size: 9 **Identification/recruitment:** Through ALS clinic		For some, ventilation limited function. LTMV was considered more a last resort (not ruled out) because of its associations above. The need for support (subsidised equipment, housing and family) affected choices regarding intervention. Financial implications were expressed more by patients than family. Communication and the ability to continue communicating was very important to patients. Patients wanted to protect family from burden but respected their opinions in decision making. However, the final say was with the patient and self-determination / autonomy was also important. There was some tension between carers wanting to make plans before patients were ready. Carers also wanted guidance about how to follow through with patient wishes. Whilst euthanasia and assisted dying were not regarded as preferable options for this sample, they did agree with withdrawal of ventilation when communication became impossible. There was a link between remaining at home and QoL, and the anticipation that IV may mean having to live in a nursing home. Fears about death were expressed, in particular regarding the fear of choking, having no air, how and when death would occur, being a burden. Such fears often haunted patients during the night, therefore assisting sleep through better ventilation (NIV or IV) was a factor in decision making. Although information was needed for decision making, there was no consensus about timing and method. Patients wanted to wait until a decision was required before accessing information, whereas carers wanted information at the onset of the disease. The decision to use NIV usually followed a crisis to do with worsening respiratory function or its

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<td>effects (e.g. lack of sleep). In contrast, decision to have IV was usually planned to avoid emergency intubation.
Decision making involves steps of adaptation and acceptance, and although ALS follows a fairly predictable disease trajectory, patients did not experience it in this way, making planning difficult.
Medical decisions to continue an intervention were also dependent on numerical outcomes (FVC) that suggested improvement following a trial period. Patients, in contrast, were not always sure how “normal” their breathing was.
Acceptance of ventilation was a lengthy process that began with familiarisation with the equipment to enable acceptance before using.
Author conclusions:
The authors suggest that supporting decision making requires a combination of providing patients and family with evidence as well as integrating patient concerns and tensions between the wishes of patients and family members. Discussions need to occur regularly to account for potential changes along the trajectory.</td>
</tr>
<tr>
<td>Martin 2012 (conference abstract)

Martin 2014 (paper)

<u>Journal paper</u> / <u>conference abstract</u>

Country: UK

<table>
<tr><td>Qualitative</td><td></td></tr>
<tr><td>Mixed method</td><td>X</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To identify factors associated with acceptance of NIV.</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients and caregivers</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td>≥ 6 months (mean 7.8 / 12.5 months (abstract), max 60 months)</td></tr>
<tr><td>Sex</td><td>49 males; 29 females</td></tr>
<tr><td>Age</td><td>Mean 62.5 (±11.8)</td></tr>
<tr><td>NIV usage</td><td>Not yet referred</td></tr>
<tr><td>Other (specify)</td><td>20.5% indicated</td></tr>
</table>
</td>
<td>Author identified themes (conference abstract):

Passive:
'no mention of intervention'
'aware of intervention but reluctant to think about it'
'passive approach'

Active:
'keen to find out more'
'intervention considered, no decision made'
'decision made to accept ' / ' decline'

Data relating to NIV provision and usage</td>
</tr>
</table>

Data collection method: Baseline physical, cognitive, psychological and health service use measures. Interviews **Theoretical underpinning:** Not reported **Sample size:** 78 patients (from 178 invited and 81 consented); 50 caregivers **Identification/recruitment**: South East ALS register (SEALS). At study enrolment, none had made a clinical decision about NIV.		awareness of NIV, but were reluctant to think about it in advance	**(conference abstract):** Two (2.6%) expressed a passive decision-making approach, believing healthcare professionals should make such decisions A firm decision at baseline was associated with uptake of NIV (10.3%) and 3.8% made a decision to refuse NIV. Participants with familial ALS were reluctant to consider interventions or made no mention of them. 21 NIV decisions (19 accepted; two refused) were made by 32 participants (41%). Most first decisions for participants with non-bulbar onset were NIV decisions (52%). NIV decisions were taken close to end-of-life (mean 2.7 months prior to death). **Conclusions (Conference abstract):** NIV tended to be offered later in the disease when people were more unwell. Despite insufficient statistical power for formal testing, findings suggest that early preferences for NIV do not always predict subsequent treatment choices. **Data relating to NIV provision and usage (paper):** 32 patients made at least one intervention decision (18 died without making a decision). 19 accepted and two refused NIV. Of those that died following a decision, NIV was decided on close to end of life (mean 2.7 months). Being more unwell at baseline (low BMI, poorer speech / swallowing) and poorer prognosis was predictive of decision making, whether for NIV or gastrostomy. Also associated with decisions were higher IQ, longer time in education and “active” approach (actively seeking information), to the two interventions. Post-decision assessment showed that being employed, understanding the illness well, having

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<td>an active approach to intervention and low depression score was associated with likelihood for refusal of intervention. Being more religious was associated with refusal at baseline and post-decision.

For carers, higher wellbeing and lower caregiver strain was associated with patient refusal of interventions. Better palliative outcome rating at baseline was most associated with patient refusal, though by post-decision this changed, possibly due to poorer outcomes based on refusal.

Author conclusions:

The results provide a framework for understanding complex factors that need to be taken into account when discussing intervention with ALS patients.</td>
</tr>
<tr>
<td>Martin 2016 (linked to Greenaway)

Journal paper / conference abstract

Country: UK

<table>
<tr><td>Qualitative</td><td>X</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To investigate decision-making re gastrostomy and NIV

Data collection method: Semi-structured interviews

Theoretical underpinning: None reported</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Health care professionals</td></tr>
<tr><td>Condition</td><td>Supporting patients with ALS</td></tr>
<tr><td>Onset</td><td>N/A</td></tr>
<tr><td>Sex</td><td>16 female, 3 male</td></tr>
<tr><td>Age</td><td>Not reported</td></tr>
<tr><td>NIV usage</td><td>5 patients had made decisions regarding NIV</td></tr>
<tr><td>Other (specify)</td><td>Of the 19, only 5 were nominated by patients using NIV. Three were respiratory Specialists, one</td></tr>
</table>
</td>
<td>Author identified themes: patient-centric factors, caregiver or family factors, and HCPs' beliefs, perspectives, and actions.

Data relating to NIV provision and usage: The patient was the main decision-maker with little evidence of caregivers playing a decisive role. The influence of professionals depended on both the approach taken and patient characteristics.

Patients were more likely to accept an intervention when they perceived few burdens, or could be reassured that any impact could be minimized. There was anxiety about the need to be admitted to hospital.

Timing - HCPs reported that many patients only agreed to an intervention when the symptoms were already significantly affecting their lives.</td>
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</table>

Sample size: 19 **Identification/recruitment:** Part of a broader study, professionals nominated by 78 patients taking part.			hospice nurse and one consultant neurologist	Challenges in timing were discussed, with consensus that it would be different for each patient considering factors such as their disease progression, social factors, emotional coping, and acceptance. **Experience of healthcare –** Previous experience could be reassuring, but for other traumatic experiences could be a major barrier. **Information –** one participant reported that patients agree to NIV simply through a lack of knowledge of any alternatives. **Positive patient traits** - active engagement in decision making, proactive coping style, active information seeking, independence, optimism, and determination. **Family –** a range of different circumstances regarding involvement of the family, the family or caregiver might influence not only the decision but also the process of decision making, in other situations caregivers seemed to have little involvement. Patient fear of a negative impact on the family was important, with positive family impact an important motivator. **Professional role –** differing viewpoints regarding the best way to approach discussion. Most described the importance of the patient being in control, although some perceived their role as the lead in discussion, not only to provide information but also to provide clear and direct guidance as to what the patient should decide. Two professionals described making decisions in the patients' best interests. The need for an individualised approach was highlighted in terms of timing, content and style. Some described

<table>
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<td>patients being presented with different opinions and information, which made it difficult to make a decision, and perhaps made them more reluctant to agree to the intervention. Professionals who held very positive opinions found it difficult to be neutral. Some perceived that taking a particular stance may help reduce the burden of decision-making for patients.

Information – Participants discussed the need for full information to be provided, including in different formats, and the right level for the patient. Content included costs, benefits, and alternatives, and the likely impact of the intervention on daily life. An emphasis was often put on the benefits to quality of life rather than prolonging life. Most believed it was the patient's understanding of the impact on his or her quality of life that determined whether or not the intervention was accepted.

Author conclusions: There is need for a "whole person" understanding of patients' decision making, as well as knowledge about the intervention itself. The paper provides a helpful summary table of implications of the study and suggested action needed.</td>
</tr>
<tr>
<td>Oliver 2016 (linked to Faull and Phelps)

Phelps 2014

Journal paper / <u>conference abstract</u>

Country: UK

<table>
<tr><td>Qualitative</td><td>X</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND / ALS</td></tr>
<tr><td>Onset</td><td>NR</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>Withdrawal</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes

Data relating to NIV provision and usage:
Phelps 2014:

Emotionality and the tensions of the situation were vivid for all. Logistics were more variably recalled; both families and HCPs held some technical aspects in great detail.

Families described a long journey to the point of</td>
</tr>
</table>

Aim of study: To look at experiences of the NIV withdrawal process **Data collection method:** Interviews **Theoretical underpinning:** Not reported **Sample size:** 17 relatives, 24 doctors and 26 nurses and allied health professionals involved in NIV withdrawal for 30 patients. **Identification/recruitment:** Not reported		decision, often triggered by loss of communication or overwhelming sense of dependence or loss of self-determination. Families often spoke of patients choosing to end life. They often sensed that professionals were inexperienced, illustrated by an absence of clear information sharing and a lack of choice. HCPs may know the patient and family well or be called upon to deliver the care with little or no previous involvement. Nurses spoke of advocacy for the patient and the family. Some felt uneasy about the decision and the withdrawal itself, often feeling professionally vulnerable. Clarity for doctors of the ethical and clinical decision- making was in contrast to the multi-layered and conflicting feelings they experienced in carrying out the patient's wishes. Medical indemnity organizations appeared unclear about the professional and legal acceptability of this and this increased the complexity and the stress of the situations. **Author conclusions:** This is a complex area of care and most HCPs are novices. Those HCPs with more experience or who are supported by experienced HCPs are better able to guide families and colleagues. Mentoring and other systems need to be developed to support those involved and improve patient outcomes. **Data relating to NIV provision and usage Oliver 2016:** Need to use medication to avoid distressing symptoms before NIV withdrawn. Additional medication administered if symptoms occurred.

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<td>HCPs intended medication doses to be sufficient to avoid symptoms - concerned that use of high doses could be seen as hastening. Most patients given morphine/ diamorphine and midazolam by subcutaneous infusion, subcutaneous injections or via an intravenous line to manage breathlessness and anxiety. Some received medication via gastrostomy.

One third experienced symptoms after NIV removed. Two cases where this required mask be temporarily replaced plus further medication. Distress experienced by some patients was difficult for all concerned.

Author conclusions: During withdrawal of NIV, distressing symptoms may occur if sedating medication doses insufficient. Presence of uncontrolled symptoms distressing to all concerned. Need for clear guidance from people with experience, to provide details of the medication required to prevent distress.</td>
</tr>
<tr>
<td>Palmer 2011

Journal paper / <u>conference abstract</u>

Country: UK

<table>
<tr><td>Qualitative</td><td></td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td>Routine data</td></tr>
</table>

Aim of study: Concordance of patients with NIV intervention

Data collection method: Retrospective case</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Patients</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>Mean 13.9 months</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>Yes</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes

N/A

Data relating to NIV provision and usage:

71% of patients were eventually concordant, 19% did not tolerate NIV and 10% died. Concordance was greater and more rapid in hospital than at home (76% vs 69%; 4.4 days vs 14.2 days respectively). NIV was tolerated well in those with symptomatic and physiological requirement (84%). 75% failure rate in physiological requirement only; 80% concordance in symptom requirement only. Most common symptom was daytime sleepiness (81%). Mean survival from</td>
</tr>
</table>

<table>
<tr>
<td>note review April 2004 – March 2011

Theoretical underpinning: NR

Sample size: 42

Identification/recruitment: NR</td>
<td></td>
<td>initiation was 10.2 months (range 0.67-84). Three patients moved from NIV to IV, one of whom survived a further 5 years.

Author conclusions:

There is a tendency for MND patients to be more concordant with NIV that is started in hospital than at home, and initiation is more rapid. Patients without symptoms are less tolerant of NIV.</td>
</tr>
<tr>
<td>Phelps 2017 (linked to Faull and Oliver)

Journal paper / conference abstract

Country: UK

<table>
<tr><td>Qualitative</td><td>X</td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To identify and explore ethical and legal issues when supporting MND patients with ventilation withdrawal.

Data collection method: Interviews (19 face-to-face; 5 telephone)

Theoretical underpinning: NR

Sample size: 24

Identification/recruitment: Through membership of associations and networks.</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Doctors (palliative care, respiratory, neurology and GPs)</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>NR</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>Yes</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes

Theoretical knowledge of ethics and law
Ethical and legal practice
Does withdrawal feel ethical and moral
Ethical and legal recommendations

Data relating to NIV provision and usage:

Settings for withdrawal: Home, hospice, hospital (acute and community), care home.

Withdrawal was rare but memorable, accompanied by emotion related to tensions at the time.

Ethics, morals and law were felt to go hand in hand. Ethical theory seemed clear but in practice was more complex (“messy”, “surreal”, “uncomfortable”).

The ethical, moral and legal right of the patient to withdrawal was acknowledged even when this could hasten death. Doctors reflected the potential to override patient wishes if patient had functional abilities, and it could be easier to do this.</td>
</tr>
</table>

		Framework for helping in this was if patient's wish was sustained over time, the patient was not depressed and had capacity to make the decision, and was making an informed choice (not influenced by others) and was aware of consequences. Establishing these factors was challenging, particularly with patient communication problems. Discussion with patient and family was very important to reach consensus in order to limit risk of legal action / media attention. Discussions were difficult when euthanasia and assisted dying came up. Discussions with colleagues was important and time consuming. Aim for individual cases to have framework applied and consensus. Some experienced dissent where colleagues felt withdrawal was akin to euthanasia and different from withdrawal of some other treatments (withdrawal seen as cause of death due to ending assistance to breath, rather than MND; drugs seen as shortening life; close timing of withdrawal and death equating to causality). Tensions could influence the setting for withdrawal and sometimes the patient's wish was not carried out. Need for greater support (ethical, moral, legal; professional and emotional) was articulated (support often from palliative care team). Consultation with ethico-legal professionals did not always help. Doctors felt responsible because of their involvement in the withdrawal. There was concern

<table>
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<td></td>
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<td>that patients asked for withdrawal because they faced further loss of ability. However, at the time of withdrawal the patient might still be alert and communicative.

Author conclusions:

Whilst ethical theory seems straight forward, in practice, doctors found this aspect very complex. Professionals need more support (perhaps from palliative care teams) in order to support the patient and family in these decisions. Advanced care planning might help reduce ambiguity but are not failsafe. Integration of palliative care and neurology might help the experiences of patients, families and professionals.</td>
</tr>
<tr>
<td>Rowe-Haynes et al 2012 (linked to Faull, Oliver and Phelps)

Journal paper / <u>conference abstract</u>

Country: UK

<table>
<tr><td>Qualitative</td><td></td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td>Cross-sectional</td></tr>
</table>

Aim of study: To identify issues and challenges doctors have encountered when withdrawing NIV in MND patients.

Data collection method: Survey

Theoretical underpinning: Not reported

Sample size: 134</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>Members of the Association of Palliative Medicine (60% directly involved in NIV withdrawal)</td></tr>
<tr><td>Condition</td><td>MND</td></tr>
<tr><td>Onset</td><td>NR</td></tr>
<tr><td>Sex</td><td>NR</td></tr>
<tr><td>Age</td><td>NR</td></tr>
<tr><td>NIV usage</td><td>Withdrawal</td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>
</td>
<td>Author identified themes

Data relating to NIV provision and usage:

5% used a protocol or guideline.

Most found the process of NIV withdrawal practically, emotionally and ethically challenging. Of those who found it very challenging, 70% reported practically challenging, 75% emotionally challenging and 60% ethically challenging.

12% found NIV very emotionally challenging. Some common difficulties included lack of guidance on practical aspects of withdrawal, poor advance care planning and the need to support all involved to prevent conflict. Statements relating to the emotional burden were diverse but suggest a significant personal impact is felt by many palliative care doctors.

Author conclusions:</td>
</tr>
</table>

<table>
<tr>
<td>Identification/ recruitment: Electronic questionnaire</td>
<td></td>
<td>Withdrawal of NIV in patients with MND appears to pose multiple challenges to palliative care doctors. Development of guidelines and a clear ethical statement of conduct may help with some of the practical and ethical challenges. Emotional issues appear more complex. Further research into the challenges faced by all professionals in the withdrawal of NIV is necessary.</td>
</tr>
<tr>
<td>Ruffell 2013

Journal paper / conference abstract

Country: UK

<table>
<tr><td>Qualitative</td><td></td></tr>
<tr><td>Mixed method</td><td></td></tr>
<tr><td>Other (specify)</td><td></td></tr>
</table>

Aim of study: To obtain HCP views about providing NIV and gastrostomy to ALS patients

Data collection method: Online survey

Theoretical underpinning: NR

Sample size: 177

Identification/recruitment: Online survey technology</td>
<td>Participant characteristics:

<table>
<tr><td>Type of group</td><td>HCPs (16 specialties)</td></tr>
<tr><td>Condition</td><td>ALS</td></tr>
<tr><td>Onset</td><td></td></tr>
<tr><td>Sex</td><td>132 female
45 male</td></tr>
<tr><td>Age</td><td>N/A</td></tr>
<tr><td>NIV usage</td><td></td></tr>
<tr><td>Other (specify)</td><td>Medical 101
Allied health 75</td></tr>
</table>
</td>
<td>Author identified themes

Response rate 13.6%

Data relating to NIV provision and usage:

76% of medical staff believed that discussion about NIV should begin after diagnosis but prior to intervention, compared to 45% allied health professionals. 48% of allied health professionals believed discussion timing should be on an individual basis.

When asked whether people with ALS have a clear idea of the effects of NIV on QoL, 29% of medical and 8% of allied health professionals disagreed with the statement.

When asked whether carers of people with ALS have a clear idea of the effects of NIV on symptoms, 41% of medical and 23% of allied health professionals were uncertain. Nearly 58% of allied health professionals agreed or strongly agreed that carers are aware of the possible effects of NIV on the patient's QoL, whilst 58% of medical staff were uncertain.

Author conclusions:

The study did not take patient dementia into account, which could account for reduced</td>
</tr>
</table>

<table>
<tr><td></td><td></td><td>compliance. Further studies need to look at the impact of ALS and dementia co-morbidity.</td></tr>
<tr><td>Saunders 2016

Country: Canada

Journal paper / conference abstract

<table><tr><td>Qualitative</td><td>X</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Other (specify)</td><td></td></tr></table>
Aim of study: To identify an ALS patient's attitude towards life-prolonging measures during various stages of disease progression, and evaluate current practices in the multidisciplinary ALS clinic.

Data collection method: Demographic data, ALSFRS-R scores, interviews.

Theoretical underpinning: Not reported

Sample size: 28

Identification/recruitment: Not reported</td><td>Participant characteristics:

<table><tr><td>Type of group</td><td>Patients</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td>NR</td></tr><tr><td>Sex</td><td>NR</td></tr><tr><td>Age</td><td>NR</td></tr><tr><td>NIV usage</td><td>Yes</td></tr><tr><td>Other (specify)</td><td></td></tr></table></td><td>Author identified themes

Data relating to NIV provision and usage:

A more positive attitude was demonstrated toward life prolonging measures as disease progressed.

Use of interventions in the clinic were evaluated over 15 years. Increasing trend in BiPAP initiation. Initiation of PAV remains constantly sparse over time.

Author conclusions:

Patients develop a more positive attitude towards life-prolonging measures as the disease progresses. Results support the multidisciplinary ALS clinic's current practices of raising the topic of interventions at multiple instances during disease progression.</td></tr>
<tr><td>Sundling 2009

Journal paper / conference abstract

Country: Sweden

<table><tr><td>Qualitative</td><td>X</td></tr><tr><td>Mixed method</td><td></td></tr><tr><td>Other (specify)</td><td></td></tr></table></td><td>Participant characteristics:

<table><tr><td>Type of group</td><td>Patients and caregivers</td></tr><tr><td>Condition</td><td>ALS</td></tr><tr><td>Onset</td><td></td></tr><tr><td>Sex</td><td>Patients: 5 male; 2 female
Caregivers: 2</td></tr></table></td><td>Author identified themes:
Getting to know your ventilator
Embracing the ventilator
Being on the ventilator on a 20-24 hour basis

Data relating to NIV provision and usage:
All but one of the patients were using NIV all night and occasionally during the day.
Contradictory emotions expressed about using</td></tr>
</table>

Aim of study: To describe patient and caregiver experiences of NIV **Data collection method:** Interviews (patients and caregivers separately) **Theoretical underpinning:** **Sample size:** 15 (7 patients and 8 caregivers who were spouses). One patient could not communicate due to 24 hour NIV. **Identification/recruitment:** Identified through hospital records. Invited through hospital (no other details).		male, 6 female **Age** Patients 45-75 years Caregivers: 40-74 years **NIV usage** 3-15 months; daily (2-20 hours) **Other (specify)**	NIV, including feelings that it had been started against their will ("*they insisted I should have one*"); feeling there was no alternative; feeling trapped in the mask. A concern was lack of knowledge about use of the NIV apart from at night, and also the ventilator not functioning optimally. Benefits from night time ventilation were increased ability to sleep at night and relaxation as soon as the mask is on. There was also less fatigue during the day, which improved the ability to carry out day to day activities. However, the mask could cause sores and different ways of dealing with these were expressed (pads, lotion, looser fitting). Patients were reluctant to use the mask in company. If at home, they would leave the room when becoming breathless, and use the mask in private. The mask could not be used at the same time as spectacles, and had to be removed for eating, showering and talking. However, NIV allowed patients to remain at home. Caregivers appreciated the benefits of sleep, rest and less anxiety that NIV gave patients, and encouraged them to use it more. Caregivers were impacted by lack of sleep due to different sleep patterns, having to help with NIV when alarms went off. They were also impacted by having to motivate patients and by not being familiar with the equipment. These impacts changed as the patients and caregiver became used to the machine. Caregivers became more relaxed because they felt the patient was safe. Caregivers reported extensive involvement in the patient's care and were unwilling to let anyone but

		a few trusted people do this. They were reluctant to leave the patient and go out in case there was a fault with the equipment or a power cut. They became adept at planning prior to transitioning between equipment, setting equipment up for transportation, so that breathing was not disrupted. They could hear when breathing was suited to a particular ventilator, and had ideas for how to improve equipment. **Author conclusions:** Patients experienced improved sleep, bodily and emotional conditions as well as being able to carry out activities when using NIV. Caregivers experienced periods of rest and lower stress but also stress from interrupted sleep with being involved intensively with the equipment. Further studies needed to assess fully the caregiver situation and also to improve ventilator and mask design.