

**Using technology to improve access to specialist care in amyotrophic lateral sclerosis: a systematic review**

Running title: Improving access to specialist care in ALS using technology

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## **Abstract**

**Objective:** To review the evidence for using technology to improve access to specialist care for patients with amyotrophic lateral sclerosis (ALS) and their carers.

**Methods:** Medline, Google Scholar and the Cochrane library were searched for articles describing technology that enabled clinical care of patients with ALS or their carers where the patient/carer and clinician were not in the same location.

**Results:** Two applications were identified: telemedicine to facilitate video conferencing as an alternative to outpatient consultations and telehealth monitoring for patients with respiratory failure. One randomised controlled trial using telehealth in patients with respiratory failure including 22 patients with ALS was identified.

Whilst rates of hospitalisation were reduced, overall mortality was unchanged and there were too few patients with ALS in the study to detect significant benefit.

**Conclusion:** There is limited evidence to support use of telemedicine or telehealth in the care of patients with ALS. Future research needs to develop an understanding of the key beneficial aspects of the traditional specialist ALS service and how these factors could be delivered using technology. Successful evaluation and implementation of technologies to facilitate access to specialist care will only be possible if all the relevant impacts of an intervention are understood and measured.

## **Introduction**

Management of a patient with amyotrophic lateral sclerosis (ALS) aims to improve quality of life and survival. Riluzole and non-invasive ventilation (NIV) can prolong life but attendance at a specialist multidisciplinary ALS clinic is also independently associated with improved survival and quality of life although the reasons for this are uncertain (1-5). Patients must travel to access these specialist services that are usually based in cities. These services often differ from those available locally, particularly in rural areas. Given the low prevalence of ALS (approximately 5.4 per 100 000) specialists cover a large geographical area and as a result, much of the day-to-day care is provided by non-specialists (6,7). In Scotland for example, six specialist nurses care for 300-400 patients covering an area of over 78 000km<sup>2</sup> (8). Lack of expertise and limited access to specialist staff and equipment causes patients and their carers to experience significant difficulties (9-14). Whilst in the UK approximately 70% of patients attend a specialist clinic at some point in their illness, patients experience difficulties travelling to clinic as well as the long duration of clinic visits (15,16). As they become more frail it often becomes impossible for them to attend the clinic and may lose the benefits offered by the specialist service.

Technologies that enable patients to access health services from their home are now used in many diseases. These include telemedicine (video conferencing), telehealth (remote monitoring of measurements such as oxygen saturations or patient symptoms), telecoaching (mentoring using phone or video) and telecare (technology to support independent living e.g. falls monitors). Other expanding areas include health “apps”, internet based education, peer support and the storage and sharing of medical records (17-19). Video conferencing has been used in neurology outpatient

settings, extensively in acute stroke thrombolysis and in palliative care, but evidence to recommend its use is limited (20-26).

Trials of telehealth in long-term conditions such as lung disease and cardiac failure have suggested that telehealth may be an acceptable way to improve access to specialist care and facilitate self-management. Reductions in mortality, decreased hospital admissions and reduced healthcare costs have been reported but benefits tend to be small and of limited clinical significance (27-29). Two large studies of telehealth reported increased mortality (30,31). One study suggested that the excess mortality could be due to an increase in healthcare interventions triggered by the telehealth monitoring (31). The other study suggested that the intervention (a self-management programme) could have resulted in a detrimental change in patients' behaviour but, it was not possible to evaluate how the intervention was implemented at each site, or whether this resulted in the excess mortality (30). This highlights the limitations of using only standard randomised controlled trials to evaluate complex telehealth interventions: without fully understanding how the intervention brings about change it is not possible to explain unanticipated effects (32).

A small number of studies using telehealth in chronic disease (e.g. asthma and heart disease) have demonstrated improvements in quality of life but many found little or no benefit (27,28,33,34). Assessment of cost-effectiveness was often limited by incomplete assessment of the cost of the intervention or health resource use (29). Even when improvements in quality of life were found, the high cost associated with the intervention meant that the cost per quality adjusted life year gained was very large (33,34).

The potential benefits and challenges of using technology to facilitate access to care in ALS differ from those in other diseases. ALS is uncommon disease requiring care from a multidisciplinary team of specialists who must address patients' changing needs, as well as supporting the use of complex equipment including that used for ventilation and gastrostomy feeding. Technology could allow a specialist team to care for patients throughout their disease regardless of patients' ability to travel to the specialist centre. However, to be successful it must be accessible to patients who may be frail, have severe disability or difficulties with communication.

## **Methods**

Our aim was to review the current technologies used to facilitate access to specialist care for patients with ALS and/or their carers. Outcomes of interest included clinical and health resource impacts but, given the novelty and complexity of these technologies, we also included papers that described the feasibility and acceptability of the intervention and impact on burden and quality of life.

### *Search strategy*

A search was conducted using Medline, Google Scholar and the Cochrane library up to the end of 2014. Three journals were hand searched: Journal of Telemedicine and Telecare, Telemedicine and e-health and the Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration journal. Relevant author, reference lists and citations from published articles were also scrutinised. The keywords and MeSH terms used were: amyotrophic lateral sclerosis, motor neurone disease, neurology, telemedicine, telehealth, remote monitoring, web, app, internet, teleneurology, respiratory failure, ventilation.

### *Selection criteria for review*

- Studies involving patients and/or carers of those with any form of ALS/motor neurone disease
- Studies using technology that enabled communication between a patient or carer and the clinician who were not in the same location
- Papers and conference abstracts reported in English describing original research or service evaluation where sufficient information was available about the intervention, population and outcome.

The quality of the study methodology was not an inclusion criteria because one aim was to identify the range and feasibility of interventions even if comparative trials were not available. The PRISMA checklist was used to guide the analysis and reporting of results (35).

## **Results**

The search strategy identified 445 academic references, of which 31 full text articles and one conference abstract were reviewed for eligibility (Figure 1). Interventions and study designs were diverse so statistical analysis was not appropriate and narrative synthesis was undertaken. The results are summarised in Tables 1-3.

Two uses for technology were identified: video conferencing (telemedicine) as an alternative to outpatient appointments and telehealth to monitor and manage patients with respiratory failure. A number of papers describing the use of internet sites for self-diagnosis, education and social networking were excluded as they did not involve communication with a care team (36). Other telemedicine programmes were identified but were excluded from the review as no evaluations had been conducted (37,38). No interventions involving carers of those with ALS were identified.

### ***Telemedicine***

Four services used videoconferencing (telemedicine) to facilitate case management (Table 1) (39-42). These were all observational studies and no formal evaluation was available. A Dutch study used an internet chat room and video link to enable four



patients to conduct individual consultations with a rehabilitation team (40).

Discussing most aspects of care using telemedicine was acceptable to patients and reduced travel to hospital, but patients still expressed a preference for face-to-face consultations when discussing emotional and psychological topics, including end-of-life decisions. Two services in the United States reported that using telemedicine had avoided outpatient visits resulting in patient travel cost savings (41,42). An Australian study described using telemedicine between a tertiary centre and local community hospitals to facilitate the care of patients living far from the ALS clinic (39). The Australian telemedicine service focused on symptom control and end-of-life care and enabled contact for an extra year with patients who would otherwise not have been able to access these services.

### ***Telehealth in respiratory failure in ALS***

#### *Study characteristics*

12 papers were identified together describing five telehealth systems used to intensively manage patients with chronic respiratory failure as an alternative to outpatient appointments. Table 2 and 3 describes the study methods and results. The interventions and studies are described first, following which the clinical, cost and feasibility outcomes are discussed.

#### *Study quality*

Only two trials were identified that involved ALS patients comparing telehealth to usual care. Only one was a randomised controlled trial, the author of which was contacted for information about the methods and results (43). Another trial was

identified which was described as randomised but actually assigned patients on the basis of their geographic location (44,45). Both trials have been included in this review but were assessed to have a high risk of bias (see Appendix 1) and neither was sufficiently powered to detect clinical or economic benefits in the ALS patients. The other papers identified were observational studies but have been included in the review because they describe the feasibility and potential economic impact of telehealth on the clinical service.

#### *Tele-assistance in patients with chronic respiratory failure*

An Italian rehabilitation service evaluated a complex telehealth system for patients with respiratory failure. Pulse oximetry data was collected and patients were assessed weekly by a respiratory nurse with access to physicians and a 24-hour emergency helpline (46).

A one-year randomised controlled trial involved 240 patients with chronic respiratory failure, 22 of whom had ALS and 50 of whom had other neurological disorders (43). 101 patients used non-invasive ventilation and 43 used tracheostomy ventilation. The primary outcome was rate of hospital admissions. Secondary outcomes included mortality, respiratory exacerbations, emergency room admissions and urgent general practitioner calls. Patients were randomised to usual care (routine three-monthly hospital appointments) or to the telehealth service with no scheduled outpatient appointments.

A five-year observational study of this telehealth service examined the staffing and financial impact of caring for 396 patients, 91 of whom had ALS (47). Two papers

describe the use of this service in ALS patients alone: a pilot, non-randomised observation study (40 patients) and a five-year service evaluation (73 patients) (48,49). It is unclear whether the same patients were involved in more than one of these studies. These evaluations estimated the resources required to run the service and potential health resource savings.

The same Italian telehealth system was used to monitor 39 patients with ALS to identify respiratory exacerbations which would trigger the provision of a mechanical insufflation-exsufflation device “Cough Assist” (50). 12 patients with ALS received cough assist on 47 occasions. The same group conducted a pilot study using long-term monitoring of peak cough flow, oxygen saturations and symptoms to identify respiratory deterioration in 12 patients with ALS using non-invasive ventilation (51). The patient recorded these measures daily and reported bi-weekly via a telephone call to a physiotherapist.

*Home telemonitoring of non-invasive ventilation in patients with amyotrophic lateral sclerosis.*

A telehealth service based in Lisbon (Portugal) caring for ALS patients used telehealth in addition to usual clinics using data collected from NIV ventilators relayed to the clinical team via the internet. A set of algorithms were developed to enable clinicians assess patients and schedule telephone calls or hospital visits (52). Forty patients with ALS commencing non-invasive ventilation were recruited into a pilot trial and economic evaluation prior to developing respiratory failure (44,45). The intervention was commenced when they started using NIV. Primary outcomes

were number of visits to hospital and number of ventilator setting changes needed to reach full compliance. Whilst the trial was described as randomised, patients were assigned a study arm according to whether they lived within Lisbon (usual hospital appointments) or outside Lisbon (intervention: telehealth plus usual three monthly appointments)(44). Furthermore, whilst limited clinical characteristics collected at baseline suggested the groups were similar, baseline health resource use, socio-economic status and co-morbid diseases were not reported.

#### *Other feasibility studies*

Two other systems used telehealth to manage patients with ALS using NIV were described in feasibility studies. Both services were felt to be feasible and acceptable to patients but no comparative trials of the services were identified (53,54).

## **Outcomes**

### *Clinical outcomes*

The Italian randomised controlled trial of 240 patients (22 of whom had ALS) reported that telehealth care was associated with significantly fewer hospitalisations, respiratory exacerbations and urgent calls to general practitioners (43). Mortality and emergency room attendance rates did not differ significantly (43). These differences only reached significance in the group of patients with chronic obstructive pulmonary disease and no significant differences were detected in the 22 patients with ALS (although the study was not powered to detect a difference in this sub-group) (43).

The Lisbon pilot trial reported that telehealth was associated with significantly fewer outpatient, emergency room and hospital visits, but conclusions should be made with caution given the limitations in methodology (44,45). There was a trend towards longer survival in the telehealth group, but median time between symptom onset and starting NIV was much longer in the telehealth group suggesting that these patients had a slower disease course than those in the control group. Therefore these results may be due survival trend to baseline differences between the groups rather than any impact from the intervention.

### *Cost*

The Italian randomised controlled trial was not powered to provide a cost-evaluation. They did suggested that given the significant reduction in hospitalisations in the telehealth group, the healthcare costs for patients using telehealth would be less, but

estimates were imprecise and no formal statistical comparison was possible (43,55). Half of all cost savings were due to a small difference in the low number of intensive care admissions (14 vs. 16) (43). Given that there were no significant differences in outcomes in the ALS patients no cost savings were demonstrated (43). However, according to the five year analysis, cost savings were made as nurses took over the roles of physicians with one nurse able to manage a caseload of 25 patients costing an estimated €105-108 per patient per month (47,49). Cost savings were also reported when the same telehealth system was used to detect respiratory exacerbations to supply Cough Assist machines (50). The service was reported to have prevented 30 hospital admissions which was estimated to be 59% cheaper than providing machines to all patients (50).

In the Lisbon study (after adjusting for survival by dividing the total health costs by the number of days using NIV) healthcare costs in the telehealth group were significantly lower due to reduced inpatient and transport costs (44,45). These results should be interpreted with caution as baseline characteristics differed and patients were assigned a study arm based on whether they lived in a rural or urban location - a factor that may independently influence health resource use.

#### *Quality of life, feasibility, acceptability and adherence*

None of the studies examined patient or carer burden or quality of life. The Lisbon study examined patients' attitudes to the service: 93% of patients rating the service as "good" or "very good" but only 36% of patients considered it to be a method of improving their life (48). The reasons for this are not described, but these telehealth regimes were very intensive requiring patients to make frequent contact with the ALS

team. The Italian study found that the majority of contacts were routine and did not result in a change in their care which may be demoralising to service users (49).

Dropout was low, but the author of the Italian study suggested (in personal correspondence) that it was difficult to recruit ALS patients to the Italian trial because they wanted to use the telehealth service and did not wish to be randomised to the control arm (43,55).

Despite the intensity of the regimes, factors that might influence patient adherence were not explored. Poor patient adherence impacted on the success of the service in the telehealth system monitoring cough to detect respiratory exacerbations. The system was so complex for the patients that they failed to adhere to the telehealth regime and did not provide sufficient readings for the system to detect a change in their condition (51). In another feasibility study using telehealth to support NIV use, those who adhered well to the telehealth regime experienced a reduction in hospitalisations, whereas those who failed to send data regularly experienced an increase in hospitalisations (54). This requires further investigation as baseline hospitalisation rates were much higher in the “good” adherence group compared to the “poor” group and no account was taken of other factors associated with compliance that may independently influence patient outcome (e.g. disease severity).

## **Discussion**

There is limited evidence to recommend the use of telemedicine or telehealth in the care of patients with ALS. However, larger evaluations of telemedicine in other neurological diseases do suggest that telemedicine could be an acceptable alternative to face-to-face consultation, particularly when travelling to clinic is difficult (21,56-

58). Using telehealth as an alternative to clinic visits appears technically feasible but further research needs to establish its safety and effectiveness. Telehealth and telemedicine could also be useful as an addition to specialist outpatient clinics. For example, telehealth could be used to better monitor patients between clinics. Telemedicine could provide access to specialist services between visits such as counselling or speech therapy or by completing some of the consultation at home thus reducing the duration of clinic visits.

With technology costs falling, if interventions do reduce health resource use they could be cost effective. The models of telehealth described in this review are intensive and require a large number of specialist staff at considerable cost, but monitoring could become more automated, reducing staff burden and making systems more affordable.

Telehealth and telemedicine services are complex interventions consisting of many component parts and their ability to bring about change depends on many factors (32). Whilst further adequately powered experimental trials are important, future research must use additional methodologies appropriate for developing and evaluating such complex interventions. Using approaches such as modelling or observational studies of interventions in practice may better identify the potential impacts on patients, staff and the clinical service, complementing any experimental studies. Such methodologies will also contribute to an understanding of factors influencing success of interventions such as the structure of different ALS services and the attitude of the patients and staff towards using new interventions.



It is also important to determine how the effects of an intervention can be comprehensively measured. This should include clinical and quality of life outcomes as well as patient and carer burden, as interventions which increase the medicalisation of patients' lives can increase burden and could have a negative effect on quality of life (59,60).

## **Conclusion**

Development of successful tele- services requires a better understanding of the beneficial aspects of the traditional ALS services and how these could be delivered using technology. There is currently limited evidence to suggest that using telehealth or telemedicine to improve access to specialist care in ALS improves outcomes or reduces costs. However, the inherent challenges of managing patients with ALS is a reason to support further exploration of how to successfully incorporate technology into ALS specialist services. Any future studies should ensure that all relevant impacts of such technology interventions are captured, enabling successful evaluation and when appropriate, future implementation.

## **Table and Figures**

Figure 1: Flow diagram of the literature search

Table 1: Telemedicine studies

Table 2: Telehealth studies

Table 3: Telehealth results and limitations

## Appendix 1: Assessment of bias summary

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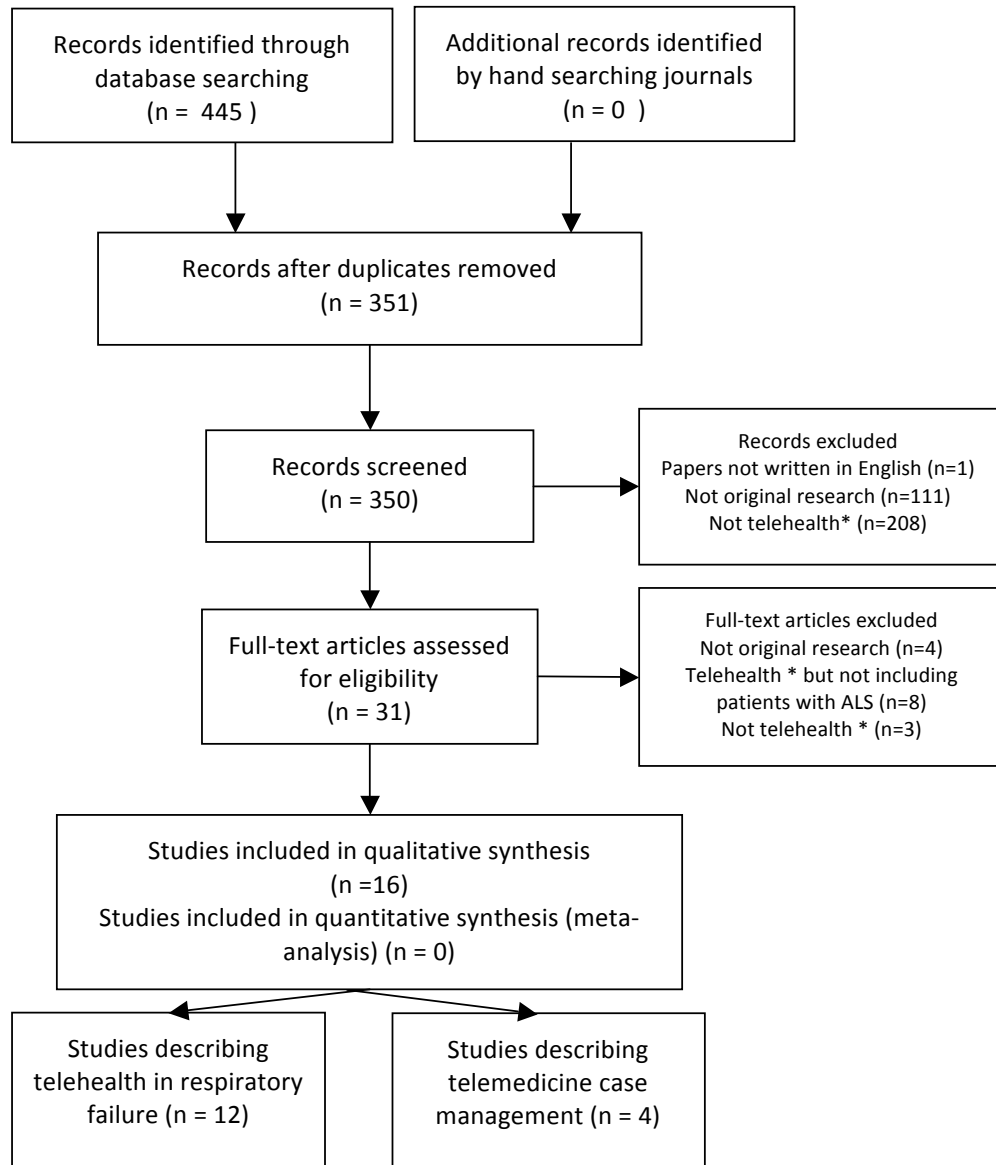
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\*telehealth refers to any intervention involving the clinical management of patients using any form of technology where the patient and the clinician were not in the same location

Table 1: telemedicine studies

<b>Title</b>	<b>Year</b>	<b>Intervention</b>	<b>Study design</b>	<b>N.o. of patients</b>	<b>Outcomes</b>	<b>Limitations</b>
<i>Tele-treatment of patients with amyotrophic lateral sclerosis (ALS)</i>	2006	Information website + scheduled access to clinician via chat room + video conferencing from tertiary hospital to home	Pilot, feasibility, acceptability	n=4	Acceptable topics for discussion: symptoms (75%), treatment options within the MND team (75%), first line and treatment options elsewhere (100%), progress (100%) Less preferred topics: acceptance/coping with MND (50%), preferences for end of life (25%)	Patients who become more disabled were unable to use equipment. All were young patients with computer experience
<i>Early and innovative symptomatic care to improve quality of life of ALS patients at Cleveland VA ALS Center</i>	2013	Video conferencing from tertiary hospital to home	Service evaluation	n=12	Predicted \$34 137 saving over two years in patient travel expenses	No formal evaluation
<i>Comprehensive care and home telehealth for veterans with ALS</i>	2013	Video conferencing from tertiary hospital to home	Service evaluation	n=17	Improved patient satisfaction and reduced driving time and travel costs (no figures provided)	No formal evaluation
<i>Telehealth in motor neurone disease</i>	2014	Telemedicine from tertiary hospital to local community hospital/health centre	Service evaluation	n=38	Allowed patients who could not travel contact with MND clinic for approx. 1 extra year	No formal evaluation

Table 2: telehealth studies

Title	Year	Intervention	Study design	Control	Time	No of patients		Patient characteristics
						Total	With MND	
<b>Tele-assistance in chronic respiratory failure patients</b>								
<i>Tele-assistance in patients with amyotrophic lateral sclerosis: long term activity and costs</i>	2012		Observational	None	Up to 5 years	n=73	n=73	25% TV, 25%NIV 34% PEG
<i>A pilot trial of telemedicine-assisted, integrated care for patients with advanced amyotrophic lateral sclerosis and their caregivers</i>	2010	Telehealth: 02 either intermittent or continuous oximetry telemetry	Observational	None	1-12 months	n=40	n=40	30% TV, 48% NIV 50% PEG
<i>Tele-assistance in chronic respiratory failure: patients' characterization and staff workload of 5-year activity</i>	2010		Observational	None	Up to 5 years	n=396	n=91	77-83% ventilated
<i>Tele-assistance in chronic respiratory failure patients: a randomized clinical trial</i>	2009	Clinical service: Specialist nurse weekly scheduled calls using clinical assessment algorithms + emergency telephone calls with physician + out-of-hours call centre who could contact physician if required. No routine outpatient clinics	RCT	3 month clinic	1 year	n=240	n=22	18% TV 43% NIV
<i>A pilot study of nurse-led, home monitoring for patients with chronic respiratory failure and with mechanical ventilation assistance</i>	2006		Feasibility	None	6 months	n=45	n=5	31% TV 52% NIV
<i>At home and on demand mechanical cough assistance program for patients with amyotrophic lateral sclerosis</i>	2010	Telehealth + clinical service as service described above CA for respiratory exacerbations	Feasibility	None	9-16 months	n=39	n=39	31% TV 38% NIV
<b>Home telemonitoring of non-invasive ventilation in patients with amyotrophic lateral sclerosis</b>								
<i>Economic cost of home-telemonitoring care for BiPAP-assisted ALS individuals</i>	2012	Telehealth: NIV ventilators monitoring usage + pattern of respiration + facility to adjust ventilator settings	Pseudo-randomised pilot	3 month clinic	Up to 3 years	n=40	n=40	100% NIV, 0% gastrostomy
<i>Home telemonitoring of non-invasive ventilation decreases healthcare utilisation in a prospective controlled trial of patients with amyotrophic lateral sclerosis</i>	2010	Clinical service: weekly review of TH data + predefined alerts (variations from +/- 1 SD of the mean values of IPAP, expiratory positive air pressure, inspiratory/ expiratory ratio, backup rate, inspiratory sensitivity, expiratory sensitivity and rise time) to alert clinicians to clinical problems + 24 hour helpline + 3 monthly clinic	Feasibility	None	Not stated	Not stated	Not stated	100% NIV
<b>Other telehealth studies</b>								
<i>Pilot study for home monitoring of cough capacity in amyotrophic lateral sclerosis: A case series</i>	2014	Telehealth: 02, PCEF, symptoms reported via email/telephone Clinical service: Bi-weekly telephone support	Pilot, observational	None	9 months	n=12	n=12	100% NIV
<i>Telemonitoring in chronic ventilatory failure: a new model of surveillance, a pilot study</i>	2012	Telehealth: 02, pulse, spirometer, CO2, BP, ventilator flow, pressure and volumes, overnight 02 Clinical service: 24-hour helpline. No routine calls	Observational feasibility	Historic data	2 years	n=16	n=3	31% TV 69% NIV
<i>A telemedicine instrument for home monitoring of patients with chronic respiratory diseases</i>	2007	Telehealth: 02, pulse, spirometer, capnometer, BP, ventilator air flow, pressure and volumes	Feasibility	None	Not stated	n=15	n=15	Using NIV/TV

TH telehealth, TV tracheostomy ventilation, NIV non-invasive ventilation, CA cough assist/mechanical insufflation-exsufflation, 02 oxygen saturations using finger probe, PCEF-peak cough expiratory force, ICU intensive care unit, PEG percutaneous gastrostomy, BP blood pressure, FVC forced vital capacity, RCT randomised controlled trial

Table 3: telehealth results and limitations

Title	Clinical outcomes	Resource use / economic evaluation / feasibility	Limitations
<p><b>Tele-assistance in chronic respiratory failure patients</b>  <i>Tele-assistance in patients with amyotrophic lateral sclerosis: long term activity and costs</i>  <i>A pilot trial of telemedicine-assisted, integrated care for patients with advanced amyotrophic lateral sclerosis and their caregivers</i></p>		<p>Estimated cost of service per patient per month: €105                      1 nurse can manage 25 patients per month                      Estimated cost of service per patient per month: €118                      19 (96%) rated TH good/very good                      7 (36%) thought TH would improve their life</p>	
<p><b>Tele-assistance in chronic respiratory failure: patients' characterization and staff workload of 5-year activity</b>  <i>Tele-assistance in chronic respiratory failure patients: a randomised clinical trial</i></p>	<p><b>TH associated with:</b>                      Fewer hospitalisations (TH 0.14 SD 0.21 per month controls 0.22 SD 0.24, p=0.01)                      Increased chance of avoiding hospital admission (p=0.004).                      Fewer respiratory exacerbations (TH 0.78 SD 0.77 per month control 0.23 SD 0.38 p=0.0001)                      Fewer urgent general practitioner calls (TH 0.22 SD 0.34 per month, control 0.07 SD 0.17 p=0.002)                      No difference in mortality, emergency room visits                      No difference in any outcome in 22 MND patients</p>	<p>Cost per patient per month €56 in year 5 (ALS patients cost more)                      Physicians' work decreased: reduced salary costs by 39% in year 1                      Estimated health costs lower in the TH group (TH mean €8907 SD €17580, control €14728, €28694) due to reduced hospitalisations                      No differences in costs in the 22 MND patients</p>	<p>High risk of bias.                      Study not powered to compare costs.                      Half cost savings due to a slightly smaller number of ICU admissions</p>
<p><b>A pilot study of nurse-led, home monitoring for patients with chronic respiratory failure and with mechanical ventilation assistance</b>  <i>At home and on demand mechanical cough assistance program for patients with amyotrophic lateral sclerosis</i></p>	<p>12 patients used CA for 47 respiratory episodes                      30 hospitalisations were avoided</p>	<p>System was feasible once problems with transmitting data were resolved by improved training of patients and carers                      Estimated cost of service per patient per month: €403 SD €420: 59% less than for providing continuous CA</p>	<p>No clinical outcomes</p>
<p><b>Home telemonitoring of non-invasive ventilation in patients with amyotrophic lateral sclerosis</b>  <i>Economic cost of home-telemonitoring care for BiPAP-assisted ALS individuals</i></p>	<p><b>TH associated with:</b>                      Fewer outpatient visits (TH 3.02, control 9.02 p&lt;0.0001)                      Fewer emergency room visits (TH 0.11, control 0.58 p&lt;0.0001)                      Fewer hospital admissions (TH 0.06, control 0.37 p&lt;0.001)                      No significant difference in survival</p>	<p><b>TH associated with:</b> no difference in estimated mean annual hospital costs (outpatient and inpatient encounters)                      TH: lower estimated costs of annual hospital service + patient transport + respiratory equipment rental (TH €8186 SD 6553, control €44143 SD 11316 p=0.005)                      Estimated total saving of €700 per patient per year                      No carer cost savings</p>	<p>High risk of bias                      Study not randomised.                      Baseline characteristics differed.                      No baseline economic data.</p>
<p><b>Implementation of a wireless device for real-time telemedical assistance of home-ventilated amyotrophic lateral sclerosis patients: a feasibility study</b>  <b>Other telehealth studies</b>  <i>Pilot study for home monitoring of cough capacity in amyotrophic lateral sclerosis: A case series</i>  <i>Telemonitoring in chronic ventilatory failure: a new model of surveillance, a pilot study</i></p>	<p>System was "feasible"</p>	<p>The system was unfeasible as compliance was poor: 22% at 6-9 months due to the complex demands of the regime on patients.</p>	
<p><b>A telemedicine instrument for home monitoring of patients with chronic respiratory diseases</b></p>	<p>73% less hospitalisations if "good" compliance (rate prior 1.222 SD 1.09 after 0.333 SD 0.5)                      100% increase in hospitalisations if "poor" compliance (prior 0.285 SD 0.487 after 0.571 SD 1.133)</p>	<p>56% patients had good adherence                      Definition of intervention adherence unclear</p>	<p>Baseline hospitalisation rates in groups different.</p>

TH telehealth, CA- cough assist/mechanical insufflation-exsufflation, ICU intensive care unit, SD standard deviation, FVC forced vital capacity. Figures reported as mean and standard deviation (SD)

## Appendix 1: Assessment of bias summary

<b>Study</b>	<b>Adequate sequence generation</b>	<b>Allocation concealment</b>	<b>Blinding</b>	<b>Incomplete outcome data addressed</b>	<b>Free of selective reporting</b>	<b>Free of other bias</b>
<i>Tele-assistance in chronic respiratory failure patients: a randomised clinical trial</i>	Low risk	Low risk	High risk	High risk	High risk	Unclear
<i>Economic cost of home-telemonitoring care for BIPAP-assisted ALS individuals</i>	High risk	High risk	High risk	Unclear	High risk	Unclear
<i>Home telemonitoring of non-invasive ventilation decreases healthcare utilisation in a prospective controlled trial of patients with amyotrophic lateral sclerosis</i>						

Based on the Risk of Bias Tool from the Cochrane Handbook for Systematic Reviews of Interventions