

A consensus review on the development of palliative care for patients with chronic and progressive neurological disease

D. J. Oliver

Palliative Medicine, Wisdom Hospice, Rochester
University of Kent, Kent, UK

G. D. Borasio

Service de soins palliatifs, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

A. Caraceni

Palliative Care Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; ^eEuropean Palliative Care Research Center NTNU, Trondheim, Norway

M. de Visser

Department of Neurology, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands

W. Grisold

Department of Neurology, Kaiser Franz Josef Hospital, Vienna, Austria

S. Lorenzl

Institute of Nursing Science and Practice, Paracelsus Medical University, Salzburg, Austria

S. Veronese

Fondazione Assistenza e Ricerca in Oncologia, Turin, Italy

R. Voltz

Department of Palliative Medicine, University Hospital, Cologne, Germany; and EAN Subspecialty Scientific Panel on Palliative Care, Vienna, Austria

Correspondence:

D.J.Oliver

Wisdom Hospice

High Bank

Rochester

Kent ME1 2NU

UK

Tel: +00441634 830456

Fax: +00 44 1634 845890

E mail: drdjoliver@gmail.com

Abstract

Background and purpose: The European Association of Palliative Care Task- force, in collaboration with the Scientific Panel on Palliative Care in Neurology of the European Federation of Neurological Societies (now the European Academy of Neurology), aimed to undertake a review of the literature to establish an evidence-based consensus for palliative and end of life care for patients with progressive neurological disease, and their families.

Methods: A search of the literature yielded 942 articles on this area. These were reviewed by two investigators to determine the main areas and the sub- sections. A draft list of papers supporting the evidence for each area was circulated to the other authors in an iterative process leading to the agreed recommendations.

Results: Overall there is limited evidence to support the recommendations but there is increasing evidence that palliative care and a multidisciplinary approach to care do lead to improved symptoms (Level B) and quality of life of patients and their families (Level C). The main areas in which consensus was found and recommendations could be made are in the early integration of palliative care (Level C), involvement of the wider multidisciplinary team (Level B), communication with patients and families including advance care planning (Level C), symptom management (Level B), end of life care (Level C), carer support and training (Level C), and education for all professionals involved in the care of these patients and families (Good Practice Point).

Conclusions: The care of patients with progressive neurological disease and their families continues to improve and develop. There is a pressing need for increased collaboration between neurology and palliative care.

Keywords

collaborative care, consensus, end of life, palliative care, progressive neurological disease

Introduction

The care of people with progressive neurological diseases is a challenge for all involved – in neurology, neurorehabilitation, general medicine and palliative care [1]. The mortality from neurological disease is increasing across Europe and progressive degenerative neurological disease is an important cause of both morbidity and disability in Europe [2]. Although there are similarities in progression, there are also specific factors for each disease, and every person will present and progress in their own individual way.

The commonest progressive neurological diseases are Parkinson's disease (PD) (prevalence of 110–180/100 000), multiple sclerosis (MS) (80–140/100 000), amyotrophic lateral sclerosis (ALS) (6–7/100 000), Huntington's disease (6/100 000), multiple system atrophy (5/100 000) and progressive supranuclear palsy (7/100 000) [3]. Stroke and primary brain tumours will also be considered within this consensus review as in many parts of Europe they come under the neurological services and present similar dilemmas in management and care. Dementia is not considered as it is managed very differently across Europe and has a specific guideline [4]. Although palliative care has been included within previous guidelines on specific diseases [5,6] there has been no overall description of the role of palliative care across many categories of progressive neurological disease.

The care of a person with progressive neurological disease will initially be within neurological services – when the diagnosis is made and initial treatment is initiated. The ongoing management of progressive neurological disease varies across Europe and can be within neurological services, neurorehabilitation, palliative care, general medical services, geriatric medicine or primary care. There is increasing involvement of palliative care services and closer collaboration with neurological services, often soon after diagnosis of a progressive disease. Palliative care provides a holistic assessment of the patient and family, considering the physical, psychological, social and spiritual aspects with a multidisciplinary team approach [7]. However, the involvement and availability of palliative care varies across Europe – between and within countries – reflecting the varying development of palliative care services and their varying involvement in non-malignant disease. Palliative care is now often considered for patients with cancer but the importance of palliative care for non-malignant disease is still developing.

The European Association of Palliative Care (EAPC) formed a taskforce to look at the palliative care within neurological disease in 2008. A collaborative approach has been undertaken with the Scientific Panel on Palliative Care of the European Federation of Neurological Societies (EFNS) – now amalgamated within the European Academy of Neurology (EAN) – to develop this paper, reviewing the evidence for the management of progressive neurological disease with the aim of establishing a consensus for recommendations on palliative and end of life care for these patients and their families. A common approach between neurology and palliative care can develop leading to a more collaborative approach to care. The EAPC and EAN are committed to increasing collaboration, with the aim of improving the care of people with neurological disease as the disease progresses and end of life approaches. This paper aims to provide evidence for the palliative care of people with neurological disease, considering all aspects of their progression.

Methods – search strategy

The search included literature on palliative care involvement in other disease groups, as we thought that there could be appropriate evidence from other areas of care. The literature review was performed by searching the following electronic databases: Medline (Ovid, PubMed), Embase (Ovid), Cinhals, Psychinfo (Ovid), the Cochrane Library.

The terms that were searched were as follows.

- 1 General palliative care terms: palliative care, specialist palliative care, terminal care, terminally ill, hospice, end of life, death, dying.
- 2 Disease-related terms: neurology, amyotrophic lateral sclerosis, motor neurone disease, Parkinson's disease, multiple sclerosis, multiple system atrophy, progressive supranuclear palsy, brain tumours.
- 3 Outcome measures: outcomes, symptoms, place of care, place of death, quality of life, caregivers, carers, needs assessment, service evaluation.

Terms listed in point 1 were combined using the Boolean term 'OR', and the same for the terms in points 2 and 3. The results of these three combinations were then combined with each other using the term 'AND'. The terms were chosen to establish the widest review of palliative care involvement in neuro- logical disease. All studies were included and the papers related primarily to neurological patients, but studies of other disease groups relevant to neurological patients were included.

This procedure was first performed in June 2006 and repeated on several occasions until May 2015, with extra references found on each occasion. The search details are shown in Fig. 1. The references included were guidelines, meta-analyses, randomized controlled trials, cohort studies and case series, and those excluded were reviews, book chapters, case reports and those relating to disease groups other than neurology unless there was a clear relevance to neurological patients such as for communication with patients and families within the publication.

Methods for reaching consensus

Two investigators (DJO, RV) looked at the literature that considered the palliative care of people with advanced neurological disease or with other progressive diseases and determined the seven main areas and the subsections. These areas were suggested from the papers included in the review, using a grounded

Results

During the appraisal of the literature seven main areas were developed from the evidence found on the management of palliative care for neurological disease. These areas have been developed further by consensus within the group theory approach, without any particular or predetermined ideas. The investigators produced the areas of care supported by the draft list of papers giving the evidence for each area. These were circulated to the other authors. The next draft was disseminated for comment – both on the areas considered and the strength of the evidence in the literature – to a wider group of health professionals. The recommendations were agreed by all authors in an iterative process and are classified and the recommendations graded according to the guidelines paper of Brainin *et al.* [8] – with

classification of the studies graded Class I to IV and recommendations graded Level A (established as effective . . .), Level B (probably effective . . .) and Level C (possibly effective . . .). There were no disagreements during this process. The initial discussions took place before the GRADE system [9] was recommended for reviewing. In this preliminary approach the development of fully evidence-based guidelines was not feasible, and this is a framework based on the appropriate evidence to answer specific clinically relevant questions and to support clinical practice. Thus, the lack of evidence for a recommendation may not necessarily reflect the actual strength and usefulness of the intervention but merely that there is little strong evidence in the literature.

Early integration of palliative care

Research within neurological care is limited but there is evidence for the effectiveness of palliative care for patients with cancer, including early palliative care increasing length of survival and reducing hospital care for patients with lung cancer ([10,11], both Class I). The development of guidelines suggesting the early integration of palliative care within cancer services has been helpful in encouraging earlier involvement ([12], Class IV).

Specialized palliative care team involvement has been shown to improve family satisfaction and symptom management and provide cost savings but the studies have limited evidence ([13], Class II).

Within the care of multiple sclerosis, early involvement of palliative care has been shown to improve symptom management and improve patient and family satisfaction ([14], Class II; [15], Class IV). There is limited evidence that palliative care input improves symptoms and overall quality of life for patients with ALS, MS and PD/multiple system atrophy/progressive supranuclear palsy ([16], Class II).

The involvement of palliative care will differ with the diagnosis and depends on the natural history of the disease. ALS has an average life expectancy of 3–5 years from symptom onset, and the symptoms and disability experienced by the patient may be profound at or soon after diagnosis, so that palliative care is often appropriate from diagnosis onwards. PD has a longer prognosis with an average of 15 years. Thus, a palliative care approach may be helpful during the progression of the disease but palliative care services may have less involvement until later in the disease progression [16].

Recommendation

Palliative care should be considered early in the disease trajectory, depending on the underlying diagnosis (Level C).

Multidisciplinary team

The involvement of a multidisciplinary team approach has been suggested in many reviews and guidelines [5] – this was considered to be a team where each member contributes his/her expertise in close cooperation with the others and could include physician, nursing, psychology/social work and allied health professionals including physiotherapist, occupational therapist, dietitian and speech and language therapist. There is limited

evidence of the effectiveness of this approach, but in Ireland it was found that ALS patients receiving care at a multidisciplinary clinic had a better prognosis – with a median survival 7.5 months longer than patients seen within general neurology clinics ([17], Class II; [18,19], Class III). A study on MS patients found increased satisfaction with multidisciplinary care ([14], Class II).

Recommendations

The assessment and care should be provided by a multidisciplinary team approach consisting of at least three different professions: physician, nurse, and social worker or psychologist/counsellor (Level C).

Patients should have a multidisciplinary palliative care assessment and access to specialist palliative care for ongoing management (Level B).

Communication

Communication and goal setting

The telling of the diagnosis of a progressive neurological disease sets the agenda for the later care of the patient and family [20]. There is evidence from the breaking of bad news in cancer that the use of a clear protocol, such as the SPIKES protocol, allows an open approach and clear discussion of the setting of goals and options of therapy and management ([21], Class IV). Studies have shown that these skills can be acquired by the use of a communication skills programme ([22], Class I). There may be specific issues in communicating with people with progressive neurological disease due to changes in the ability to speak and cognitive impairment.

Advance care planning

Research from the care of patients with cancer has shown that the use of advance care planning can help the later care of patients ([23], Class I) and models to aid this discussion and planning have been suggested ([24], Class I). These principles have been used within the care of people with neurological care ([25], Class IV) and a study has suggested that patients do wish advance care planning to be adhered to ([26], Class IV). A survey amongst severely affected MS patients expressed their wish to discuss the progression of their disease with their doctors and doctors who avoided such discussions were considered to be less empathetic ([27], Class IV).

Recommendations

Communication with patients and families should be open, including the setting of goals and therapy options, and should be structured following validated models (Level C).

Early advance care planning is strongly recommended, especially when impaired communication and cognitive deterioration are possible as part of disease progression (Level C).

Symptom management

There is increasing evidence that palliative care involvement may improve both quality and

length of life for people with cancer ([10], Class I). There is limited evidence of the effectiveness of palliative care for neurological disease in improving quality of life or patient or family satisfaction but studies have shown an improvement in quality of life and symptoms and patient and family satisfaction for ALS ([16], Class II) and MS ([14], Class II).

Within neurological disease there is limited evidence of the effectiveness of careful assessment and management of all aspects of care – physical, psychological, social and spiritual – as part of a palliative care approach: ALS ([6], Class IV), MS ([28], Class IV), PD ([29,30], Class IV), glioblastoma ([31], Class IV), stroke ([32], Class IV) and Huntington’s disease ([33], Class IV).

Recommendations

Physical symptoms require thorough differential diagnosis, pharmacological and non-pharmacological management and regular review (Good Practice Point).

Proactive assessment of physical and psychosocial issues is recommended to reduce the intensity, frequency and need for crisis intervention (unplanned care) (Level B).

The principles of symptom management, as part of the wider palliative care assessment, should be applied to neurological care (Level B).

Carer support

The care of a person with a progressive neurological disease often causes stress – physical and emotional – for carers, whether family or non-family carers. Coping with the relentless loss of functional abilities associated with neurological disease and the effects of these losses may be the cause of depression and a reduced quality of life for the person ([34,35], Class III). Careful assessment and appropriate support may be helpful in reducing caregiver burden and the effects on the carers ([36], Class IV; [37], Class III). The effects of coping with cognitive change may be particularly profound ([38], Class IV). Psychosocial support is necessary following the death, in providing bereavement support and counselling, as appropriate to the family’s needs ([39], Class II). Clear communication with carers and families is helpful in providing the knowledge they need to cope with the deteriorating condition. It is clear that not only the primary care-giver but also families of persons with ALS need more supportive interaction and information during the patients’ illness and their end of life ([40], Class IV). Professional carers may also experience increased caregiver burden with prolonged involvement and care of people with progressive neurological disease. There may be feelings of impotence and meaningless coping with the disease progression and facing patient and family coping with continual loss ([41], Class II). This may present as depression, stress or burnout (emotional exhaustion, depersonalization and reduced personal accomplishment) if there is no understanding or action taken to reduce the stresses that may occur ([42], Class IV). Appropriate training and support can be helpful in reducing the risks of burnout and other emotional distress ([43], Class II; [44], Class II).

Recommendations

The needs of carers should be assessed on a regular basis (Level C).

The support of carers – before and after death – is an indispensable part of palliative care as it may reduce complicated bereavement and improve patients' quality of life (Level C).

Professionals involved in the care of progressive disease should receive education, support and supervision to reduce the risks of emotional exhaustion and burn-out (Level C).

End of life care

The recognition of deterioration in disease progression near the end of life is essential in enabling the provision of appropriate care and support for patients and their families. Regular reassessment is important, with careful continued discussion to enable the changes to be recognized ([45], Class IV). Triggers have been suggested for the recognition of end of life for patients with progressive neurological disease – swallowing problems, recurring infection, marked decline in functional status, first episode of aspiration pneumonia, cognitive difficulties, weight loss and significant complex symptoms ([46], Class IV). These are being further evaluated but there is evidence that these triggers may help in the recognition of the end of life – with increasing numbers of triggers identified as death approaches ([47], Class III). In PD there is evidence that loss of weight and a lessening in effectiveness of medication may suggest that palliative care should be considered ([48], Class III).

Although patients and families may have fears of a distressing death from progressive neurological disease, there is evidence that this is rare with good palliative care and support ([49], Class IV). Families do appreciate honesty and awareness of deterioration. Symptoms and other issues can be managed effectively by a multidisciplinary team with experience of specialist palliative care, and death for the majority of patients is peaceful ([49,50], both Class IV).

Patients and families may wish to discuss hastened death – by euthanasia or physician-assisted suicide ([51,52], Class IV). In the Netherlands up to 31% of people with ALS consider euthanasia or physician-assisted suicide, although 69% of these people follow this through ([53], Class IV). The availability of these options varies from country to country and in most areas they are not considered to be part of palliative care. However, the discussion of these issues should be open and can allow patients and families to talk of their fear and concerns about dying and death ([54,55], both Class IV). These patients may fear distress and pain during the dying process or may be wishing to retain control over their life and death, thus expressing their own autonomy ([56], Class III; [57], Class IV). These discussions may be ongoing considering a patient's possible adaptation processes in the course of a fatal disease ([58], Class IV), and patients, families, carers and professional carers may need continuing support ([59], Class III).

The recognition of the final stages of dying – over the last few days of life – can be useful in allowing the focus of care to be clarified and a palliative care approach initiated ([60], Class II; [61], Class III). There is evidence that the regular review of patient care and the recognition of the final stages of life encourage the appropriate multidisciplinary management of the patient and family, including the management of symptoms, provision of medication, psychosocial support of the patient and family and consideration of spiritual issues ([60], Class II; [61], Class III).

Recommendations

Continued and repeated discussion with patients is essential due to changes in function – physical and cognitive – and preferences (Level C)

Encourage open discussion about the dying process and explain that most patients will die peacefully with appropriate care (Level C).

Encourage open discussion of wishes to restrict treatment and interventions and the wish for hastened death, and assess regularly (Level C).

Recognition of deterioration over the last weeks and months is relevant for the appropriate management (Level C).

The diagnosis of the start of the dying phase, although this may not always be possible, is relevant for the appropriate management, including the use of appropriate medication and intervention and care and support of families and carers (Level C).

Training and education

There is little in the education and training of medical students, doctors in training and neurologists, and the wider multidisciplinary team concerning the palliative care approach to patients and families ([46,62,63], all Class IV), although there are examples of excellence [64]. Moreover, there is limited education in the care of patients with progressive neurological patients within the training of specialists in palliative medicine. These skills, particularly in communication ([20,64], both Class I) can be learnt and there is evidence, particularly from the care of cancer patients, of the improvement in skills with the appropriate training and experience. A targeted education programme for health professionals improved understanding about end of life care for people with motor neurone disease ([65], Class IV).

Recommendations

Palliative care principles should be included in the training and continuing education of neurologists (Good Practice Point).

The understanding and management of neurological symptoms of patients in the advanced stages of neuro- logical diseases should be included in the training and continuing education of specialist palliative care professionals (Good Practice Point).

Conclusion

There is increasing evidence of the integration of palliative care in the care of patients with progressive neurological disorders [66]. This review shows that there is limited evidence for the provision of palliative care for patients with progressive neurological disease and the recommendations have limited support from the literature. However, there would appear to be increasing evidence that palliative care and an improved approach to the communication with and support of patients and their families does lead to improved care and patient experience.

There is increased awareness of the approaches with guidelines which have been developed across Europe [67]. For example in the UK NICE guidelines on the use of non-invasive ventilation in motor neurone disease [68] there is discussion about the need for the consideration of end of life issues throughout the process of monitoring and establishing treatment. In the European guidelines on ALS [6] palliative and end of life care are highlighted as an important area of care.

However, there is pressing need to consider the role of palliative care in the management of all progressive neurological diseases. This will involve not only palliative care services and neurology but also primary care, rehabilitation services and other medical and professional services. There is particular interaction with rehabilitation medicine, as there is often an overlap in areas of care provided, particularly when there is a slowly progressive disease [67]. The issues of collaboration and interaction with other disciplines, and within disciplines, are complex and would benefit from further research, with the aim of clarifying the most appropriate way of supporting patients and families, without adding to their interaction with multiple caring teams.

This paper is a step in the ongoing development with the aim of encouraging all involved in this area of care to look at the most appropriate and evidence-based management so that the quality of life of patients and families can be maximized. As there was limited evidence from this review a further wide literature review and clear evidence-based approach using the GRADE protocols would be helpful in establishing and confirming this consensus review. There would appear to be a lack of good evidence to support the recommendations and further research into this area of care is urgently needed.

Acknowledgements

The authors would like to acknowledge the many people who commented on and contributed to this paper, in particular R. Burman, Consultant in Palliative Medicine and Honorary Senior Lecturer at the Cicely Saunders Institute, King's College London, UK.

Disclosure of conflicts of interest

The authors have no specific conflicts of interest to the production of this document. They are all involved in research projects on neurological disease and have written widely on this subject. However, this involvement has not affected the document, as no specific medication or intervention is recommended.

References

1. Borasio GD. The role of palliative care in patients with neurological disease. *Nat Rev Neurol* 2013; 9: 292–295.
2. World Health Organisation. Global burden of neurological disorders: estimates and projections. In: Aarli JA, Avanzini G, Bertolote JM, *et al.*, eds. *Neurological Disorders Public Health Challenges*. Geneva, Switzerland: World Health Organisation, 2006: 27–39.
3. Oliver D, Silber E. End of life care in neurological disease. In: Oliver D, ed. *End of Life Care in Neurological Disease*. London: Springer, 2012.
4. Hort J, O'Brien JT, Gainotti G, *et al.* EFNS guidelines for the diagnosis and management of Alzheimer's disease. *Eur J Neurol* 2010; 17: 1236–1248.
5. Miller RG, Jackson CE, Karsarkis EJ, *et al.* Practice Parameter update: The care of the patient with amyotrophic lateral sclerosis: multidisciplinary care, symptom management, and cognitive/behavioural impairment (an evidence-based review). *Neurology* 2009; 73: 1227–1233.
6. Andersen PM, Abrahams S, Borasio GD, *et al.* The EFNS task force on diagnosis and management of amyotrophic lateral sclerosis. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS) revised report of an EFNS task force. *Eur J Neurol* 2012; 19: 360–375.
7. World Health Organization. *Palliative care*. 2002. <http://www.who.int/cancer/palliative/definition/en/> (accessed 01/09/2013)
8. Brainin M, Barnes M, Baron JC, *et al.* Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. *Eur J Neurol* 2004; 11: 577–581.
9. Guyatt GH, Oxman AD, Vist GE, *et al.* GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *Br Med J* 2008; 336: 924–926.
10. Temel JS, Greer JA, Muzikansky A, *et al.* Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 2010; 19: 733–742.
11. Bakitas M, Lyons KD, Hegel MT, *et al.* Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer; the Project ENABLE II randomised controlled trial. *JAMA* 2009; 19: 741–749.
12. Gaertner J, Wolf J, Hallek M, Glossmann J-P, Voltz R. Standardising integration of palliative care into comprehensive cancer therapy – a disease specific approach. *Support Care Cancer* 2011; 19: 1037–1043.
13. Zimmermann C, Riechelmann R, Krzyzanowska M, Rodin G, Tannock I. Effectiveness of specialized palliative care: a systematic review. *JAMA* 2008; 299: 1698–1709.
14. Edmonds P, Hart S, Gao W, *et al.* Palliative care for people severely affected by multiple sclerosis: evaluation of a novel palliative care service. *Mult Scler* 2010; 16: 627–636.
15. Higginson IJ, McCrone P, Hart SR, Burman R, Silber E, Edmonds PM. Is short-term palliative care cost-effective in multiple sclerosis? A randomized phase II trial. *J Pain Symptom Manage* 2009; 38: 816–826.
16. Veronese S, Oliver D. *Palliative Care for People with Neurodegenerative Conditions*. Saarbrücken: Lambert Academic Publishing, 2013.
17. Traynor BJ, Alexander M, Corr B, Frost E, Hardiman O. Effect of a multidisciplinary amyotrophic lateral sclerosis (ALS) clinic on ALS survival: a population-based study, 1996–2000. *J Neurol Neurosurg Psychiatry* 2003; 74: 1258–1261.
18. Aridegbe T, Kandler R, Walters SJ, Walsh T, Shaw PJ, McDermott C. The natural history of motor neuron disease: assessing the impact of specialist care. *Amyotroph Lateral Scler Frontotemporal Degener* 2013; 14: 13–19.
19. Rooney J, Byrne S, Heverin M, *et al.* A multidisciplinary clinic approach improves survival in ALS: a comparative study of ALS in Ireland and Northern Ireland. *J Neurol Neurosurg Psychiatry* 2015; 86: 496–503.

20. Borasio GD, Sloan R, Pongratz DE. Breaking the news in amyotrophic lateral sclerosis. *J Neurol Sci* 1998; 160 (Suppl. 1): S127–S133.
21. Baile WF, Buckman R, Lenzi R, Glober G, Beale EA, Kudelka AP. SPIKES – A six step protocol for delivering bad news: application to the patient with cancer. *Oncologist* 2000; 5: 302–311.
22. Lienard A, Merckaert I, Libert Y, *et al.* Is it possible to improve residents breaking bad news skills? A randomised study assessing the efficacy of a communication skills training programme. *Br J Cancer* 2010; 103: 171–177.
23. Jacobsen J, Robinson E, Jackson VA, Meigs JB, Billings JA. Development of a cognitive model for advance care planning discussions: results from a quality improvement initiative. *J Palliat Med* 2011; 14: 331–336.
24. Jacobsen J, Jackson V, Dahlin C, *et al.* Components of early outpatient palliative care consultation in patients with metastatic non-small cell cancer. *J Palliat Med* 2011; 14: 459–464.
25. Voltz R, Akabayashi A, Reese C, Ohi G, Sass HM. End-of-life decisions and advance directives in palliative care: a cross cultural survey of patients and health-care professionals. *J Pain Symptom Manage* 1998; 16: 153–162.
26. Jox RJ, Krebs M, Bickhardt J, Hessdorfer K, Roller S, Borasio GD. How strictly should advance decisions be followed? The patients' opinion *Palliat Med* 2008; 22: 675–676.
27. Buecken R, Galushko M, Golla H, *et al.* Patients feeling severely affected by multiple sclerosis: how do patients want to communicate about end-of-life issues? *Patient Educ Couns* 2012; 88: 318–324.
28. Golla H, Galushko M, Pfaff H, Voltz R. Unmet needs of severely affected multiple sclerosis patients: the health professionals' views. *Palliat Med* 2011; 26: 139–151.
29. Lee MA, Prentice WM, Hildreth AJ, Walker RW. Measuring symptom load in idiopathic Parkinson's disease. *Parkinsonism Relat Disord* 2007; 13: 284–289.
30. Hasson F, Kernohan WG, McLaughlin M, *et al.* An exploration into the palliative and end-of-life experiences of carers of people with Parkinson's disease. *Palliat Med* 2010; 24: 731–736.
31. Walbert T, Khan M. End of life symptoms and care in patients with primary malignant tumours: a systematic literature review. *J Neurooncol* 2014; 117: 217–224.
32. Payne S, Burton C, Addington-Hall J, Jones A. End-of-life issues in acute stroke care: a qualitative study of the experiences and preferences of patients and families. *Palliat Med* 2010; 24: 146–153.
33. Travers E, Jones K, Nichol J. Palliative care provision in Huntington's disease. *Int J Palliat Nurs* 2007; 13: 125–130.
34. Miyashita M, Narita Y, Sakamoto A, *et al.* Care burden and depression in caregivers caring for patients with intractable neurological diseases at home in Japan. *J Neurol Sci* 2009; 276: 148–152.
35. Trail M, Nelson ND, Van JN, Appel SH, Lai EC. A study comparing patients with amyotrophic lateral sclerosis and their caregivers on measures of quality of life, depression, and their attitudes toward treatment options. *J Neurol Sci* 2003; 209: 79–85.
36. Gelfman LP, Meier DE, Morrison RS. Does palliative care improve quality? A survey of bereaved family members. *J Pain Symptom Manage* 2008; 36: 22–28.
37. Aarsland D, Larsen JP, Karlsen K, Lim NG, Tandberg E. Mental symptoms in Parkinson's disease are important contributors to caregiver distress. *Int J Geriatr Psychiatry* 1999; 14: 866–874.
38. Caap-Ahlgren M, Dehlin O. Factors of importance to the caregiver burden experienced by family caregivers of Parkinson's disease patients. *Aging Clin Exp Res* 2002; 14: 371–377.
39. Kissane DW, McKenzie M, Bloch S, Moskowitz C, McKenzie DP, O'Neill I. Family focussed grief therapy: a randomised controlled trial in palliative care and bereavement. *Am J Psychiatry* 2006; 163: 1208–1218.
40. Cipolletta S, Amicucci L. The family experience of living with a person with amyotrophic lateral sclerosis: a qualitative study. *Int J Psychol* 2015; 50: 288–294.
41. Morita T, Murata H, Kishi E, Miyashita M, Yamaguchi T, Uchitomi Y. Meaninglessness in terminally ill

- cancer patients: a randomised controlled study. *J Pain Symptom Manage* 2009; 37: 649–658.
42. Pereira SM, Fonseca AM, Carvalho AS. Burnout in palliative care: a systematic review. *Nurs Ethics* 2011; 18: 317–326.
 43. Fillion I, Duval S, Dumont S, *et al.* Impact of meaning-centred intervention on job satisfaction and on quality of life among palliative care nurses. *Psychooncology* 2009; 18: 1300–1310.
 44. Gouveia MC, Oliver DJ. Can emotional support for health care workers to cope with death anxiety reduce burnout and improve patient care. *J Palliat Care* 2011; 27: 287–295.
 45. Neudert C, Wasner M, Borasio GD. Patients' assessment of quality of life instruments: a randomised controlled trial of SIP, SF-36 and SEIQoL-DW in patients with amyotrophic lateral sclerosis. *J Neurol Sci* 2001; 191: 103–109.
 46. End of life care in long term neurological conditions: a framework for implementation. National End of Life Care Programme 2010.
 47. Hussain J, Adams D, Allgar V, Campbell C. Triggers in advanced neurological conditions: prediction and management of the terminal phase. *BMJ Support Palliat Care* 2014; 4: 30–37.
 48. Richfield EW, Jones EJS, Alty JE. Palliative care for Parkinson's disease: a summary of the evidence and future directions. *Palliat Med* 2013; 27: 805–810.
 49. O'Brien T, Kelly M, Saunders C. Motor neurone disease: a hospice perspective. *Br Med J* 1992; 304: 471–473.
 50. Bausewein C, Hau P, Borasio GD, Voltz R. How do patients with primary brain tumour die? *Palliat Med* 2003; 17: 558–559.
 51. Voltz R, Galushko M, Walisko J, *et al.* Issues of 'life' and 'death' for patients receiving palliative care – comments when confronted with a research tool. *Support Care Cancer* 2011; 19: 771–777.
 52. Stutzki R, Weber M, Reiter-Theil S, Simmen U, Borasio GD, Jox RJ. Attitudes towards hastened death in ALS: a prospective study of patients and family caregivers. *Amyotroph Lateral Scler Frontotemporal Degener* 2014; 15: 68–76.
 53. Maessen M, Veldink JH, Onwuteaka-Philipsen BD, *et al.* Euthanasia and physician-assisted suicide in amyotrophic lateral sclerosis: a prospective study. *J Neurol* 2014; 261: 1894–1901.
 54. Ganzini L, Johnston WS, McFarland BH, Tolle SW, Lee MA. Attitudes of patients with amyotrophic lateral sclerosis and their care givers toward assisted suicide. *N Engl J Med* 1998; 339: 967–973.
 55. Bascom PB, Tolle SW. Responding to requests for physician-assisted suicide: 'These are uncharted waters for both of us'. *JAMA* 2002; 288: 91–98.
 56. Ganzini L, Goy ER, Dobscha SK. Oregonians' reasons for requesting physician aid in dying. *Arch Intern Med* 2009; 169: 489–492.
 57. Maessen M, Veldink JH, van den Berg LH, Schouten HJ, van der Wal G, Onwuteaka-Philipsen BD. Requests for euthanasia: origin of suffering in ALS, heart failure and cancer patients. *J Neurol* 2010; 257: 1192–1198.
 58. Lule D, Nonnenmacher S, Sorg S, *et al.* Live and let die: existential decision processes in a fatal disease. *J Neurol* 2014; 261: 518–525.
 59. Ganzini L, Harvath TA, Jackson A, Goy ER, Miller LL, Delorit MA. Experiences of Oregon nurses and social workers with hospice patients who requested assistance with suicide. *New Engl J Med* 2002; 347: 582–588.
 60. Di Leo S, Beccaro M, Finelli S, Borreani C, Constantini M. Expectations about and impact of the Liverpool Care Pathway for the Dying Patient. *Palliat Med* 2011; 25: 293–303.
 61. Veerbeek L, van Zuylem L, Swart SJ, *et al.* The effect of the Liverpool Care of the Dying: a multi-centre study. *Palliat Med* 2008; 22: 145–151.
 62. Carver AC, Vickrey BG, Bernat JL, Ringel SP, Foley KM. End-of-life care: a survey of US neurologists' attitudes, behavior and knowledge. *Neurology* 1999; 53: 284–293.
 63. American Academy of Neurology. Palliative care in neurology. The American Academy of

Neurology Ethics and Humanities Subcommittee. *Neurology* 1996; 46: 870–872.

64. Szmulowicz E, El-Jawahri A, Chiappetta L, Kamdar M, Block S. Improving residents' end-of-life communication skills with a short retreat: a randomised controlled trial. *J Palliat Med* 2010; 13: 439–452.
65. McConigley R, Aoun S, Kristjanson L, *et al.* Implementation and evaluation of an education program to guide palliative care for people with motor neurone disease. *Palliat Med* 2012; 26: 994–1000.
66. Turner-Stokes L, Sykes N, Silber E, Khatri A, Sutton L, Young E. From diagnosis to death: exploring the interface between neurology, rehabilitation and palliative care in managing people with long-term neurological conditions. *Clin Med* 2007; 7: 129–13
67. Bede P, Oliver D, Stodart J, *et al.* Palliative care in amyotrophic lateral sclerosis: a review of current inter- national guidelines and initiatives. *J Neurol Neurosurg Psychiatry* 2011; 82: 413–418.
68. National Institute for Health and Care Excellence. Clinical Guideline 105: Motor Neurone Disease; the use of non-invasive ventilation in the management of motor neurone disease. NICE July 2010.

Figure 1 Selection of studies for the review.

