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*Study Protocol* · **Open Access** ·

# Hospital without dyspnea: rationale and design of a multidisciplinary intervention

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**Abstract**

Dyspnea is a common and disabling symptom of respiratory and heart diseases, which is growing in incidence. During hospital admission, breathlessness is under-diagnosed and under-treated, although there are treatments available for controlling the symptom. We have developed a tailored implementation strategy directed to medical staff to promote the application of these pharmacological and non-pharmacological tools in dealing with dyspnea. The primary aim is to decrease the rate of patients that do not receive an adequate relief of dyspnea. This is a four-stage quasi-experimental study. The intervention consists in two teaching talks that will be taught in Cardiology and Respiratory Medicine Departments. The contents will be prepared by Palliative Care specialists, based on available tools for management of dyspnea and patients' needs. A cross-sectional study of dyspnea in hospitalized patients will be performed before and after the intervention to ascertain an improvement in dyspnea intensity due to changes in medical practices. The last phase consists in the creation of consensus protocols for dyspnea management based in our experience. The results of this study are expected to be of great value and may change clinical practice in the near future and promote a changing for the better of dyspnea care.

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## 1 Background

Breathing difficulty is the most typical and common symptom of heart failure and lung diseases.[1–3] Often this symptom is under diagnosed and patients do not receive an adequate treatment.[3,4] Moreover, dyspnea is a poor prognostic factor and also carries mental and functional impairments in patients who suffer from it.[5,6] In fact, the symptom dimension transcends the physical to the emotional sphere with remarkable decline in the quality of life.[7]

There are now treatments that have shown a significant improvement of dyspnea when added to standard treatment, such as opioids,[3,6] but routine use of these tools in daily practice is not extended, and physicians' attitudes towards prescribing opioids for refractory dyspnoea vary widely, mainly due to fears about side effects.[4,8] However, the relief of dyspnea should be considered a right of the patient within the healthcare received.[9] Other non-pharmacological tools are widely extended and utilized by patients and families, such as oxygen supplementation,[10] ventilators and non-conventional medicines, even though their efficacy seems to be more than questionable.

Dyspnea in heart failure has often a multifactorial origin and, in the majority of cases, persists even after pulmonary congestion has been successfully treated.[11] Opioid therapy has widely been implemented in Palliative Care units. Its beneficial effects largely exceed the expectable harmful effects. The most feared one is respiratory depression, but it is uncommon in patients who present strong pain or dyspnea.[12] The most frequent side effects, such as constipation, drowsiness and nausea, often get better after dosage adjustment or adjuvant medications implementation (laxatives and antiemetic drugs). Moreover, sedative effects of opioids can be useful for reducing tachypnea and respiratory distress.

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The benefit of opioid treatment for dyspnea in heart failure has been suggested in several trials with a decrease in the intensity of the symptom, quality of life improvement, and better exercise performance.[13–15]

In the next years, an increase in the prevalence of dyspnea is expected, given the appearance of new treatments that have prolonged survival of patients with advanced heart disease and chronic obstructive pulmonary disease. Due to this reason, more patients will have to live with a chronic refractory dyspnea (CRD),[15,16] and occasional acutely exacerbations, also called irruptive dyspnea (ID).[5,17] They will also present frequent hospital admissions due to this reason.[5,14,17]

In order to improve the management of patients with dyspnea in our centre, we formed a multidisciplinary working group that involves three departments (Palliative Care, Cardiology, and Respiratory Medicine). A protocol intervention was designed to estimate the magnitude of the problem and to perform changes in daily clinical practice, aimed for improving dyspnea in patients with advanced heart failure and in those with pulmonary disease.

The control of dyspnea in patients with advanced cancer has recently been studied in a randomized controlled trial.[18] This same project continues currently assessing the symptomatic impact and costs savings of these interventions on dyspnea of non-advanced cancer patients. It will help to evaluate the effectiveness and efficiency of the use of pharmacological and non-pharmacological measures in this setting.[10,19] As there are few references in the literature of learning models to improve the management of dyspnea,[20,21] we have designed a diffusion model of skills specifically addressed to medical and nursing staff. In this regard, this is an original and innovative proposal. This method might be a breakthrough for dissemination of therapeutic strategies for healthcare professionals.[18,22] We decided to apply the specific model of cancer dyspnea in palliative care.[18,23] There are also some studies of learning approaches addressed to palliative care's nurses that have resulted effective, specifically in cancer patients with chronic pain.[24–26]

In 2014, we conducted two pilot experiences of transfer of knowledge in the palliative management of dyspnea. Two teaching sessions were presented in the Departments of Respiratory Medicine and Cardiology. The great acceptance among cardiologists, respiratory medicine specialists and the rest of medical staff, encouraged us to develop this initiative, which is detailed below. Furthermore, in 2013 the Palliative Care Unit has been responsible for teaching about pain management intervention in the "Comprehensive Care Program pain associated with end stage renal disease in dialysis units". A preliminary analysis has shown promising results: more than half of patients experienced a significant pain relief after medical workout.

In 2010, the American College of Chest Physicians published a consensus document which concerns the management of dyspnea in patients with advanced pulmonary or heart disease, which has provided the basis of our approach.[27]

## 2 Objective

Our main aim is to decrease the rate of the following primary outcomes: (1) rate of patients with advanced heart and respiratory diseases that present CRD and do not receive adequate symptomatic relief during hospital admission; and (2) rate of patients with advanced heart and lung diseases that present ID and do not receive adequate rescue medication.

Our secondary aims are: (1) to detect the prevalence, intensity and functional impact of dyspnea (CRD and ID) in patients admitted to our hospital; (2) to describe the therapeutic tools (pharmacological and no pharmacological) employed for symptomatic treatment of dyspnea; (3) to improve diagnosis and therapeutic skills of medical staff regarding dyspnea treatment; (4) To evaluate the subjective perception of CRD and ID of our patients and the impact associated with an implementation of educational talks addressed to medical staff; (5) to ascertain whether a specific educational talk would be cost-effective for dyspnea management, based on previous experiences on chronic pain in oncology patients; and (6) to evaluate the efficacy and the side effects derived from a chronic treatment with opioids for CRD and ID.

When we refer to dyspnea relief we should keep in mind that a strategy aimed at reducing intensity is more realistic that a complete healing. There is general consensus on the evaluation of this subjective symptom by Verbal Numerical Scale 0–10,[28] taking into account that often dyspnea intensity is more important than functional capacity and a 1/10 relief in the score or 20% of the initial value is clinically significant in the RCD. However, 2/10 relief is required in the same scale in ID.[16]

## 3 Methods

### 3.1 Design

A quasi-experimental study plus cross-sectional study of dyspnea in hospitalized patients has been planned. Educational talks will be conveyed to medical staff of our hospital in the Departments of Cardiology and Respiratory Medicine

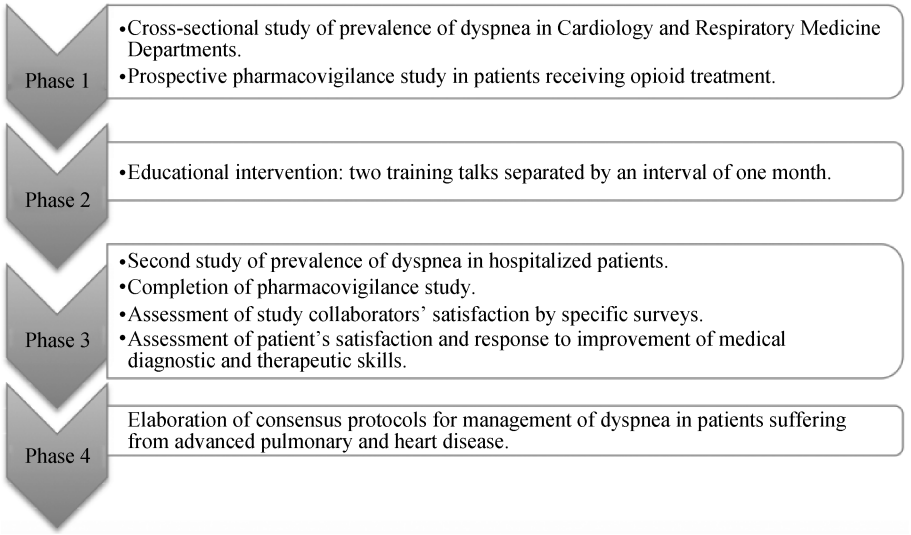


**Figure 1. Project phases.**

directed to the improvement of quality of life and breathlessness reduction. We will join forces with the Palliative Care Department for a permanent active cooperation in order to provide a comprehensive care of patients with dyspnea. Furthermore, we have planned a prospective pharmacovigilance phase for patients receiving treatment with opioids.

### 3.2 Setting

This project will take place in a University hospital. Our target population are patients admitted with chronic heart failure, chronic obstructive respiratory disease or other respiratory processes presenting with an exacerbation episode. The candidates will be selected by consecutive sampling. Every patient that meets the inclusion criteria will be included until reaching the sample size of 100. The inclusion and exclusion criteria can be viewed in Table 1.

### 3.3 Usual care

Patients admitted to Respiratory Medicine and Cardiology units will receive the appropriate treatment for exacerbation, according to evidence-based Clinical Guidelines.[29,30] Routine medications may include diuretics, vasodilators, bronchodilators, antibiotics, corticosteroids or other deemed necessary by doctors. Non-pharmacological measures, such as mechanical or non-invasive ventilation, oxygen supplementation and diagnostic/therapeutic procedures will be carried out: echocardiography, coronary angiography, bronchoscopy, blood tests, chest X-rays or other required according to medical judgement. Psychological support to patients and families will also be offered.

**Table 1. Inclusion and exclusion criteria.**

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|---|
| Inclusion criteria |
| Hospital admission with dyspnea as main symptom |
| Acceptance of participation in the study |
| Diagnosis of chronic respiratory disease |
| Diagnosis of chronic heart failure |
| Dyspnea with CRD higher than 1/10 and ID higher than 2/10 degree by Rating Numerical Scale |
| Exclusion criteria |
| Cognitive impairment |
| Voluntary dropout |

CRD: chronic refractory dyspnea; ID: irruptive dyspnea.

### 3.4 Intervention

Our study is divided in four phases, with two educational talks taught by experts on Palliative Care Medicine (Figure 1). These talks will mark a before and an after of the project. We propose a comprehensive approach, with combined non-pharmacological and pharmacological measures and periodic reassessment of patient's symptoms. These measures will be provided in addition to standard treatment. Opioids will be prescribed in an optimized manner for those patients requiring it, with an individualized adjustment of dosage and periodic counselling.

Those patients requiring post-discharge medical supervision will be scheduled for a date in day hospital. Day hospital is a healthcare platform that enables medical assistance during several hours on an outpatient basis. Blood analysis and chest X-ray are performed and, most importantly, changes and adjustment of medication are made. This close monitoring can avoid hospital readmissions but also it would be the best way to adjust opioid dosage (titration or lowering if needed) and solve the patient and family's queries.

The main objective of this approach is a reduction of intensity and disability associated with dyspnea, also promoting the patient self-management of the symptom. None intervention itself guarantees the relief of dyspnea but multimodal assessment by physical, psychological and pharmacologic means improves the patient's mastery and wellbeing.[26]

The first step of this process is the training of the medical staff. Doctors and nurses take care of breathless patients during hospital admission, when the symptoms are acutely exacerbated. Unfortunately, dyspnea is an under diagnosed condition, so patients are often undertreated. Hospitalization is a singular chance to introduce a change in habits in patients and families, so doctors must be able to recognize the symptom and start the treatment. The educational program is expected to improve the medical response. The contents will be standardized and divided in three areas: general knowledge, attitudes and skills. Two interventions of 2 h duration will be provided, in order to reinforce the information and solve queries. The slides and a practical summary will be given to the audience.

The educational program is designed to improve general knowledge, attitude, and skills. This will be done in the following way: (1) General knowledge. Description of dyspnea mechanisms in order to give a better understanding of the physiological and psychological causes. Dyspnea therapies apply this basic physiological and cognitive knowledge for patient relief in daily practice (i.e., opioid counterbalancing response to sympathetic overactivity). (2) Attitude. A high level of motivation and commitment is desirable. Communication skills will be reinforced. We will convey psychological support in all phases of the trial. Physicians and nursing staff must be able to identify and anticipate problems and manage the patient's symptoms. Patients should take part in the decisions that affect them. The importance of daily clinical assessment of dyspnea intensity by validated tools [such as Numerical Rating Scale (NRS) and modified Borg Dyspnea Scale] will be underlined. (3) Skills. During this educational programme clinical cases based on daily practice will be discussed. Working in groups will enable the exchange of ideas and proposals. Physicians and nursery staff will be encouraged to expose their own clinical challenges.

Non-pharmacological tools will also include these interventions: behavioural therapy, self-management reinforcement, tailored exercise, family psychotherapy and communication and day hospital visits. The results of these measures will be assessed by periodical evaluations of the program.

### 3.5 Pharmacologic treatment

Opioid therapy will be started after informed consent, including advice regarding side effects and their management. There is no unanimous agreement about the initial dose or opioid type utilisation,[23] but it is reasonable to prescribe the lower dose to keep the symptoms under control and individualise according to patients characteristics and response.

Anxiolytic medications will also be added on individual bases. Opioid treatment will be increased gradually if needed. Patient symptoms should be evaluated during hospital admission and after dosage adjustment, taking into account treatment efficacy and side effects. The opioid selected in our study is morphine sulphate due to previous experience and broad use. Other morphine derivatives (such as codeine, tramadol and oxycodone) will be used as second choice in selected patients. In those suffering from irruptive dyspnea short-acting preparations of low dose morphine (2–3 mg every 6 h) will be used to subjugate the crisis. In patients affected predominantly by refractory dyspnea long-acting and sustained release formulations will be preferred, taking an initial dose of 5 mg twice daily. Changes in dosage will be performed only if the patient remains symptomatic. If the patient is taking a sustained release formulation, the dose will be increased by 5 mg each time and therapeutic benefit will be assessed in a two-week period. For those patients receiving an immediate release or short-acting formulation, the titration dose used will be a 1 mg increase over the previous dose, every week until an effective dose is achieved.

### 3.6 Prospective pharmacovigilance study

During phases 1 and 3, we will perform a pharmacovigilance study. Oral and parenteral morphine is currently considered the opioid of choice in the management of dyspnea in palliative care,[31,32] and there is abundant literature that supports it use, but the data-sheet limits it outside of pain indications to cardiogenic dyspnea, and procedural anxiety. Therefore, and although it is not essential for the project, we added a pharmacovigilance study to our design. Such studies are being carried out recently in the context of palliative care when they have unquestionable efficacy data from certain drugs, and seek to confirm known data security in the long-term employment.[33]

During the pharmacovigilance phase, we will assess the following variables: (1) Number of patients that receive opioid treatment at three months of inclusion; (2) opioid dosage; (3) changes of dosage; and (4) adverse effects derived from opioids that lead to discontinuation of treatment

### 3.7 Recruitment

An informed consent will be administered to each patient before the interview. All patients must give voluntary consent to use their clinical data for the purpose of the study,

but they will receive the treatment or interventions in accordance with the standard practice in any case. The patients included will no perceive financial reward whether they sign consent or not.

The information collected for the study will be treated according to the provisions of established norms regulating patient autonomy and obligations regarding clinical information and documentation, with particular respect to privacy of the participants.

### 3.8 Data collection

The patients will be included the same day of hospital admission. It is difficult to define a simple size, as the number of variables that will be assessed is high. However, a total of about 100 subjects are expected to be needed. Regarding the study of the effect of the educational intervention on the intensity of dyspnea, to detect a difference of 1 point on the NRS, with a standard deviation of 2.22, a statistical power of 0.90 and an alpha value of 0.05, 39 subjects are needed.

We have developed a data sheet including those variables required for the cross-sectional study in both phases (before and after educational talks). The variables that will be assessed are listed in the next paragraph. Investigators of Cardiology and Respiratory Medicine Departments will pass a questionnaire to patients admitted on the first 24 h of admission.

The evaluating tools we have selected include well-validated dyspnea scales, quality of life and functional capacity indexes and measurements of respiratory and cardiac parameters, listed in Table 2. We will measure the impact of dyspnea by both unidimensional Numerical Rating Scales and the Medical Research Council scale to estimate the impact on daily activities.

**Table 2. Evaluating tools.**

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| Severity and functional impact | Unidimensional measure of overall dyspnea: NRS<br>Impact on basic daily live activities: MRC.[33] |
| Health-related quality of live | Measures of quality of life related to HRQOL such as SF-12 or EQ-5 |
| Functional capacity | Measures of functional capacity—Karnofsky Index, BMI, NYHA classification |
| Mood state | Anxiety and depression: hospital anxiety and depression scale |
| Palliative measure needs | Palliative outcome scale |
| Unidimensional measurement of the intensity of pain | Numerical rating pain scale |

BMI: body mass index; EQ-5: EuroQuol 5; HRQOL: health related quality of Life; MRC: medical research council; NRS: numerical rating scale; NYHA: New York Heart Association; SF-12: short form 12 health survey.

During the cross-sectional phase, the following variables will be assessed. Independent variables: (1) demographic data: age, sex; (2) Charlson comorbidity index; (3) main clinical diagnosis and etiology of chronic lung or heart disease; (4) non-pharmacological interventions for dyspnea management: position, environment, ventilators, humidifier, non-invasive mechanical ventilation, supplementary oxygen, etc; (5) pharmacological interventions: opioids consumption (expressed by morphine equivalent daily dose), benzodiazepines consumption (expressed by midazolam equivalent daily dose); (6) laboratory parameters (haemoglobin levels); (7) functional capacity by New York Heart Association class; (8) functional parameters: left ventricular ejection fraction in chronic heart failure, forced expiratory volume in chronic respiratory diseases; (9) functional status: Karnofsky scale, body mass index; (10) quality of life: Short Form 12 Health Survey (SF-12), Euroquol; (11) palliative needs: Profile of Moods Scale; (12) mood and depression state: Hospital Anxiety and Depression Scale; and (13) pain: Numerical Rating scale.

Dependent variables: (1) presence of CRD and ID; (2) dyspnea intensity; (3) functional impact of dyspnea; and (4) impact of dyspnea on quality of life.

### 3.9 Statistical analysis

During the cross-sectional phase (study of dyspnea prevalence), we will use descriptive statistics to describe the study population. We have established the following categories for analysis: (1) dyspnea with a Numerical Rating Scale score over 1 point in CRD and over 2 points in ID; and (2) any dyspnea amenable for pharmacological treatment (a score of 3 or 4 on the scale modified Medical Research Council dyspnea).

The assessment of the effect of the educational intervention will be analysed through multiple linear regression and a multiple logistic regression model adjusting for other qualitative variables acting as possible confounders (sex, age, underlying disease, etc).

### 3.10 Phases

The project is set around a classic model of quasi-experimental study of transfer of knowledge "observation-educational intervention-observation". The design also includes a study of prevalence of dyspnea and pharmacovigilance of opioids treatment.

We are aware of the challenge of trying to modify habits and behaviours in a dynamic environment like the hospital. This implies a prior systematic analysis and establishment of critical priorities, as well as the possible causes of the "usual" clinical behaviours.

This project will be divided in 4 phases (Figure 1). Phase 1: evaluation in the Cardiology and Respiratory Medicine Departments. Cross-Sectional study. During this phase, we will estimate the prevalence and severity of dyspnea in patients admitted to the hospital with heart failure or respiratory disease exacerbation. Phase 2: teaching Intervention conducted by Palliative Care specialists in both departments. The objective is to achieve an improvement in diagnostic and therapeutic skills of doctors and nurses who take care of these patients. Phase 3: evaluation of the impact of the teaching intervention in both departments and pharmacovigilance study. Phase 4: development of consensus protocols Cardiology-Respiratory Medicine-Palliative Care for dealing with dyspnea. Reduce the incidence of patients who suffer from CRD or ID, and develop rescue strategies is a priority in these departments.

### 3.11 Budgets and estimated costs

The estimated costs are those inherent of hospitalisation and may vary according to the medical centre. The teaching intervention is not expected to increase significantly the health care spending and is highly feasible, because it will promote making a better use of system resources already available.

## 4 Discussion

Nowadays, we have several tools available for dealing with our patient's breathlessness, but underused.[5] It's therefore regrettable that one of the reasons of this therapeutic apathy is the lack of knowledge and experience of the medical staff.[34] We propose an innovative method to enhance the medical training on dyspnea, so patients will experience an improvement in quality of life. With this design we try to apply methods that have proved effective in other Palliative Care related areas, such as oncological pain.[26] As we previously stated, quality interventions of knowledge transfer have a powerful and positive impact in medical skills and reflected in patients' relief.

One of the objectives of our project is the elaboration of multidisciplinary consensus protocols. In the future, we hope to further extent these protocols to other hospital services, such as geriatrics or internal medicine, and even to primary health care, where the prevalence of CRD is very high. A fluid and close communication between practitioners and families is highly desirable, and being aware of the needs of patients dealing with chronic dyspnea might prevent undesirable hospital admissions for symptoms exacerbations.

This is an innovative model of medical training in dyspnea management, a widespread problem. We propose a multidisciplinary approach including pharmacological treatment with drugs with a well-known potential benefit, such as opioids, and also non-pharmacological measures (i.e., chest physiotherapy and behavioural therapy). The study will start in 2016, and the first data analysis will be available in 2017.

## References

1 Simon ST, Higginson IJ, Benalia H, *et al*. Episodes of breathlessness: types and patterns—a qualitative study exploring experiences of patients with advanced diseases. *Palliat Med* 2013; 27: 524–532.
2 Parikh RB, Kirch RA, Smith TJ, Temel JS. Early specialty palliative care—translating data in oncology into practice. *N Engl J Med* 2013; 369: 2347–2351.
3 Mahler DA, O'Donnell DE. Recent advances in dyspnea. *Chest* 2015; 147: 232–241.
4 Johnson MJ, Abernethy AP, Currow DC. Gaps in the evidence base of opioids for refractory breathlessness. A future work plan? *J Pain Symptom Manage* 2012; 43: 614–624.
5 Hui D, Morgado M, Vidal M, *et al*. Dyspnea in hospitalized advanced cancer patients: subjective and physiologic correlates. *J Palliat Med* 2013; 16: 274–280.
6 Currow DC1, Abernethy AP. Pharmacological management of dyspnoea. *Curr Opin Support Palliat Care* 2007; 1: 96–101.
7 Moens K, Higginson IJ, Harding R. Are there differences in the prevalence of palliative-care related problems in people living with advanced cancer and eight non-cancer conditions? A systematic review. *J Pain Symptom Manage* 2014; 48: 660–677.
8 Viola R, Kiteley C, Lloyd NS, *et al*. The management of dyspnea in cancer patiets: a systematic review. *Support Care Cancer* 2008; 16: 329–337.
9 Currow DC, Abernethy AP, Ko DN. The active identification and management of chronic refractory breathlessness is a human right. *Thorax* 2014; 69: 393–394.
10 Johnson MJ, Abernethy AP, Currow DC. The evidence base for oxygen for chronic refractory breathlessness: issues, gaps and a future work plan. *J Pain Symptom Manage* 2013; 45: 763–775.
11 The official statement of the American Thoracic Society. Dyspnea. Mechanisms, assessment, and management: a consensus statement. *Am J Respir Crit Care Med* 1999; 159: 321–340.
12 Oxberry SG, Bland JM, Clark AL, *et al*. Repeat dose opioids may be effective for breathlessness in chronic heart failure if given for long enough. *J Palliat Med* 2013; 3: 250–255.
13 Williams SG, Wright DJ, Marshall P, *et al*. Safety and potential benefits of low dose diamorphine during exercise in patients with chronic heart failure. *Heart* 2003; 89: 1085–1086.
14 Johnson MJ, McDonagh TA, Harknessc A, *et al*. Morphine for the relief of breathlessness in patients with chronic heart

failure—a pilot study. *Eur J Heart Fail* 2002; 4: 753–756.
15 Currow DC, Higginson IJ, Johnson MJ. Breathlessness–current and emerging mechanisms, measurement and management: a discussion from an European Association of Palliative Care workshop. *Palliat Med* 2013; 27: 932–938.
16 Johnson MJ, Bland JM, Oxberry SG, *et al*. Clinically important differences in the intensity of chronic refractory breathlessness. *J Pain Symptom Manage* 2013; 46: 957–963.
17 Simon ST, Bausewein C, Schildmann E, *et al*. Episodic breathlessness in patients with advanced disease: a systematic review. *J Pain Symptom Manage* 2013; 45: 561–578.
18 Farquhar MC, Prevost A, McCrone P, *et al*. Is a specialist breathlessness service more effective and cost-effective for patients with advanced cancer and their carers than standard care? Findings of a mixed-method randomised controlled trial. *BMC Med* 2014; 12: 194.
19 Farquhar MC, Prevost AT, McCrone P, *et al*. Study protocol: phase III single-blinded-fast-track pragmatic randomised controlled trial of a complex intervention for breathlessness in advanced disease. *Trials* 2011; 12: 130.
20 Kamal AH, Miriovsky BJ, Currow DC, Abernethy AP. Improving the management of dyspnea in the community using rapid learning approaches. *Chron Resp Dis* 2012; 9: 51–61.
21 Abernethy AP, Kamal AH, Wheeler JL, Cox C. Management of dyspnea within a rapid learning healthcare model. *Curr Opin Support Palliat Care* 2011; 5: 101–110.
22 Godycki-Cwirko M, Zakowska I, Kosiek K, *et al*. Evaluation of a tailored implementation strategy to improve the management of patients with chronic obstructive pulmonary disease in primary care: a study protocol of a cluster randomized trial. *Trials* 2014; 15: 109.
23 Mahler DA. Opioids for refractory dyspnea. *Expert Rev Respir Med* 2013; 7: 123–134.
24 Phillips JL, Heneka N, Hickman L, *et al*. Impact of a novel online learning module on specialist palliative care nurses' pain assessment competencies and patients' reports of pain: results from a quasi-experimental pilot study. *Palliat Med* 2014; 28: 521–529.
25 Dahlin C. It takes my breath away end-stage COPD. Part 2: pharmacologic and nonpharmacologic management of dyspnea and other symptoms. *Home Healthc Nurse* 2006; 24: 218–224.
26 Cummings GG, Armijo Olivo S, Biondo PD, *et al*. Effectiveness of knowledge translation to improve cancer pain management. *J Pain Symptom Manage* 2011; 41: 915–939.
27 Mahler DA, Selecky PA, Harrod CG, *et al*. American College of Chest Physicians consensus statement on the management of dyspnea in patients with advanced lung or heart disease. *Chest* 2010; 137: 674–691.
28 Hjermstad MJ1, Fayers PM, Haugen DF, *et al*; European Palliative Care Research Collaborative (EPCRC). Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manage* 2011; 41: 1073–1093.
29 Vestbo J, Hurd SS, Agustí AG, *et al.* Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2013; 187: 347–365.
30 Yancy CW, Jessup M, Bozkurt B, *et al*. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013; 62: 147–239.
31 Currow DC, McDonald C, Oaten S, *et al*. Once-daily opioids for chronic dyspnea: a dose increment and pharmacovigilance study. *J Pain Symptom Manage* 2011; 42: 388–399.
32 Simon ST, Koskeroglu P, Bausewein C. Pharmacological therapy of refractory dyspnoea: a systematic literature review. *Schmerz* 2012; 26: 515–522.
33 Crawford GB, Agar MM, Quinn SJ, *et al*. Pharmacovigilance in hospice/palliative care: net effect of haloperidol for delirium. *J Palliat Med* 2013; 16: 1335–1341.
34 Hadjiphilippou S, Odogwu SE, Dand P. Doctors' attitudes towards prescribing opioids for refractory dyspnoea: a single-centred study. *BMJ Support Palliat Care* 2014 Mar 6. [Epub ahead of print].
35 Bestall JC, Paul EA, Garrod R *et al*. Usefulness of the Medical Research Council (MRC) dyspnea scale as a mesaure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999; 54: 581–586.