Review Article

A Comparison of Symptom Prevalence in Far Advanced Cancer, AIDS, Heart Disease, Chronic Obstructive Pulmonary Disease and Renal Disease

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Abstract

Little attention has been paid to the symptom management needs of patients with life-threatening diseases other than cancer. In this study, we aimed to determine to what extent patients with progressive chronic diseases have similar symptom profiles. A systematic search of medical databases (MEDLINE, EMBASE, and PsycINFO) and textbooks identified 64 original studies reporting the prevalence of 11 common symptoms among end-stage patients with cancer, acquired immunodeficiency syndrome (AIDS), heart disease, chronic obstructive pulmonary disease, or renal disease. Analyzing the data in a comparative table (a grid), we found that the prevalence of the 11 symptoms was often widely but homogeneously spread across the five diseases. Three symptoms—pain, breathlessness, and fatigue—were found among more than 50% of patients, for all five diseases. There appears to be a common pathway toward death for malignant and nonmalignant diseases. The designs of symptom prevalence studies need to be improved because of methodological disparities in symptom assessment and designs. J Pain Symptom Manage 2006; 58–69. *© 2006 U.S. Cancer Pain Relief Committee. Published by Elsevier Inc. All rights reserved.*

Key Words

Cancer, AIDS, heart disease, chronic obstructive pulmonary disease, renal disease, palliative care, terminal care, end of life, symptoms, prevalence

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Introduction

Populations are aging all over the world,[1–3] with those aged 60 and over growing faster than any other age group.[1] By 2025, the percentage of people aged 65 years and over will be almost 30% in developed and almost 15% in less developed regions.[2,3] While this increase in longevity is welcome, as a consequence more and more people are dying from chronic, rather than acute, diseases.[4–6] They will usually have endured several symptom complexes for many years. Cartwright,[7] for example, compared reports of the last year of life in 1969 and 1987. In the later study,

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people died at an increased age, but their longer life was associated with prolonged unpleasant symptoms.

The symptom management and end-of-life strategies pioneered over the past four decades by hospices and palliative care services have focused mainly on cancer patients.[8–10] Little attention has been paid to patients with other life-threatening diseases,[9,11] even though these cause three of four deaths in developed countries. Some studies have suggested that people with noncancer conditions experience a similar degree of symptom distress as cancer patients, and would benefit from a more holistic, inclusive, and supportive care network.[12–14] Indeed, one of the first studies on dying, by Hinton[15] in 1963, described how physical and mental distress were more pronounced in patients dying from heart or renal failure than those with cancer. As a result, governmental and other reports have urged that palliative care be extended to patients with progressive, incurable, nonmalignant conditions.[16]

However, a simple expansion of existing models of care to include all noncancer diseases may not be appropriate. Apart from acquired immunodeficiency syndrome (AIDS), noncancer patients are on average older than cancer patients,[17] have different patterns of dependency[18] and functional decline, and are likely to be suffering from comorbidities. Little is known about their symptom experiences and, in particular, how these compare with those of cancer patients. For example, do noncancer patients have the same complexity of symptoms as cancer patients? Are there new and different symptoms affecting those with noncancer conditions? What is the relevance of knowledge about symptom management in cancer for noncancer conditions?

In this study, we sought to determine, from existing studies, the prevalence of 11 symptoms (pain, depression, anxiety, confusion, fatigue, breathlessness, insomnia, nausea, constipation, diarrhea, and anorexia) among end-stage patients suffering from five common, chronic, and progressive conditions—cancer, AIDS, heart disease (HD), chronic obstructive pulmonary disease (COPD), and renal disease (RD). We aimed to determine whether patients with different diseases have different profiles of symptoms.

Methods

Search Strategy

We searched three electronic databases, MEDLINE (1966 to June, 2004), EMBASE (1988 to June, 2004), and PsycINFO (1985 to June, 2004), using three groups of keywords:

1. *Symptoms, pain, confusion, delirium, cognitive failure, depression, low mood, sadness, anxiety, dyspnoea, dyspnea, breathlessness, fatigue, weakness, anorexia, nausea, diarrhoea, diarrhea, constipation, insomnia, poor sleeping* (selected as the most appropriate terms to target the 11 symptoms);
2. *Dying, end of life, terminally ill, hospice, palliative care, terminal care* (terms selected to identify samples of patients at the end of life);
3. *Terminal disease, advanced cancer, metastatic cancer, AIDS, end stage heart disease, end stage heart failure, end stage respiratory disease, end stage chronic obstructive pulmonary disease, end stage COPD, end stage renal disease (RD), end stage renal failure* (terms selected to identify our specified disease groups).

Within each group the keywords were combined using *or.* The resultant three groups were then combined using *and.*

For the purpose of this review, different ways of assessing symptoms were considered. Given the variety of terms used in articles and textbooks to designate symptoms, we used more than one keyword for most of the symptoms—*delirium* and *cognitive failure* were used as alternative search terms for confusion; *dyspnoea* or *dyspnea* for breathlessness; *low mood* and *sadness* for depression; *weakness* for fatigue; and *poor sleeping* for insomnia.

We also searched relevant chapters in 12 textbooks of palliative care, internal medicine, and oncology: *Oxford Textbook of Palliative Medicine*; *Handbook of Psychiatry in Palliative Medicine*; *Palliative Care for Non-Cancer Patients*; *Clinical Audit in Palliative Care*; *Palliative Medicine Secrets*; *Managing Terminal Illness*; *A Guide to Symptom Relief in Palliative Care*; *Oxford Handbook of Dialysis*; *Cancer Pain: Assessment and Management*; *Gastrointestinal Symptoms in Advanced Cancer Patients*; *Issues in Palliative Care Research*; *Oncology for Palliative Medicine* (Appendix). Reference lists of articles and chapters were checked to refine the search for important previous work on the theme (e.g., articles surrounding large samples, systematic reviews, and/or meta-analysis). Because the majority of studies reported on cancer patients and few on other conditions, more extensive searching and follow-up were undertaken for the four nonmalignant conditions.

Inclusion/Exclusion Criteria

We included studies where the target population encompassed adults with advanced illness suffering from cancer, AIDS, HD, COPD, or RD *and* for whom the prevalence of specified symptoms had been calculated. For the purpose of this study, advanced illness was taken to include patients who were described as having advanced or terminal illness, were in hospice care, had deteriorated despite treatment, or who were deemed to have a poor prognosis by investigators (i.e., less than one year).

We excluded articles addressing any restricted population, such as patients with specific cancer types, single cancer sites, children, and drug users; articles reporting symptoms from only the very last hours of life, e.g., the terminal 48 hours; and case reports of single patients. Papers not written in English, Spanish, and Portuguese were excluded due to the investigators' limits of translation.

Data Extraction

Data were extracted to predesigned summary tables under the following headings: *authors*, *country of origin*, *year of publication*, *aims of the study*, *number of participants (sample size)*, *study design*, *measurement methods*, and *prevalence of individual symptoms.*

Analysis

Extracted data were transferred to each cell of a "palliative symptom grid" to contrast information about symptom prevalence for the five chosen terminal conditions (Table 1). The number of patients across studies was calculated for each cell—for each of the symptoms under each diagnosis. When no data were found for a specific symptom and condition, "—" was displayed in the grid. Because of variability in assessment tools, samples sizes, and accrual models, it was not possible to reliably combine the findings of different studies. Therefore, we summarized the prevalence ranges for each symptom in each disease category, allowing the findings to be appraised in terms of the minimum and maximum reported prevalences.

Results

In total, 1900 articles were found from the electronic searches. Of these and follow-up of the reference lists, 64 eligible articles were identified (33 cancer, 9 AIDS, 2 HD, 3 COPD, 13 RD, and 4 considered more than one disease) and reference lists were searched. In addition, information was extracted from 18 book chapters.

Table 1 shows the results extracted from our palliative care grid, in terms of minimum and maximum prevalences for each symptom within the five selected clinical conditions. Most studies, particularly large-scale studies, describe symptoms for cancer patients. For this reason, the prevalences of symptoms in cancer are related to a much higher number of patients (ranging from 2,888 to 10,379 patients, for each symptom), when compared with all the other four diseases (ranging from 19 to 1,435 patients). No data were obtained for the prevalence of nausea and diarrhea among COPD patients, nor for confusion among RD patients. Hence, "—" is displayed for such cases. For some symptoms and conditions, we found only one eligible data source, and thus can only report a single prevalence. That was the case for insomnia and anorexia among AIDS patients; anxiety and diarrhea among HD patients; and diarrhea among renal patients.

There were wide variations in symptom prevalence. Figs. 1 and 2 illustrate this in more detail and plot the symptom prevalence results for all included studies for depression and breathlessness.

Appraisal of the study methods identified variables that may account for the wide range of prevalence found. These are illustrated in Table 2 for the symptom of depression. Many of these factors were also noted for other symptoms, where ranges were narrower but still present. Nevertheless, our findings highlighted that depression is common not only among cancer patients, but also nearly equally among AIDS, HD, COPD, and renal patients (77% against 82%, 36%, 71%, and 60%, respectively,

Table 1

Symptom Prevalence, Summarized from the Palliative Symptom Grid

Symptoms	Cancer	AIDS	HD	COPD	RD
Pain	35–96%[7,8,11,19,33–47] N =10,379[a]	63–80%[48–50] N = 942	41–77%[22,34,51,52] N = 882[a]	34–77%[4,22,53] N = 372	47–50%[54,55] N = 370
Depression	3–77%[7,11,19,20,33,36,41,43,45,47,56–63] N = 4378[a]	10–82%[50,61,64,65] N = 616[a]	9–36%[52,66] N = 80[a]	37–71%[4,53] N = 150	5–60%[67–72] N = 956[a]
Anxiety	13–79%[19,33,36,41,45,47,58,62,63] N = 3274	8–34%[12,64,73] N = 346[a]	49%[52] N = 80	51–75%[74] N = 1008	39–70%[67,68] N = 72[a]
Confusion	6–93%[7,19,20,34,36,39,42–47,60,75–81] N = 9154[a]	30–65%[76,82] N = ?[a]	18–32%[22,34,52] N = 343[a]	18–33%[4,22] N = 309	—
Fatigue	32–90%[8,24,35,41–43,45,47,63,83] N = 2888[a]	54–85%[50,84] N = 1435	69–82%[8,22,52] N = 409	68–80%[22,53] N = 285	73–87%[71,85] N = 116
Breathlessness	10–70%[7,8,11,19,33–36,39–47,61,86–88] N = 10,029[a]	11–62%[50,88] N = 504	60–88%[8,22,34,51,52,61] N = 948[a]	90–95%[4,22,53,61] N = 372[a]	11–62%[55,89] N = 334
Insomnia	9–69%[7,8,11,19,33,39,41–43,45,47] N = 5606	74%[50] N = 504	36–48%[8,52] N = 146	55–65%[4,53] N = 150	31–71%[55,85,90] N = 351
Nausea	6–68%[8,11,19,33–36,39–47,61,91–93] N = 9140[a]	43–49%[50,94] N = 689	17–48%[8,34,52] N = 146[a]	—	30–43%[85,95,96] N = 362
Constipation	23–65%[7,11,19,33–35,39–45,47,50,93] N = 7602[a]	34–35%[50,94] N = 689	38–42%[34,52] N = 80[a]	27–44%[4,53] N = 150	29–70%[97] N = 483
Diarrhea	3–29%[11,33,39–41,43,44,47,61,92,93,98] N = 3392[a]	30–90%[50,61,98,99] N = 504[a]	12%[52] N = 80	—	21%[71] N = 19
Anorexia	30–92%[7,8,11,19,33,35,39–46,92,93,100] N = 9113	51%[50] N = 504	21–41%[8,52] N = 146	35–67%[4,53] N = 150	25–64%[89,96] N = 395

1. Minimum-maximum range of prevalence (%) is shown.
2. HD = heart disease; COPD = chronic obstructive pulmonary disease; RD = renal disease.
3. *N* refer to the total number of patients involved in the studies found for each symptom in a given disease (e.g., there are 372 patients involved in the three studies on pain prevalence in COPD).
4. Superscripted numbers relate to the reference source and indicate the number of studies for each symptom in a given disease (e.g., there are three studies on pain prevalence in COPD patients). In two occasions, a single study reported a prevalence range rather than a single point prevalence—anxiety for COPD and constipation for renal failure. "—" was displayed when no data were found for a specific symptom and condition (e.g., confusion for renal failure).

[a] The number of patients is underestimated or unknown because prevalence figures given by textbooks were considered (for which the number of patients was not provided).

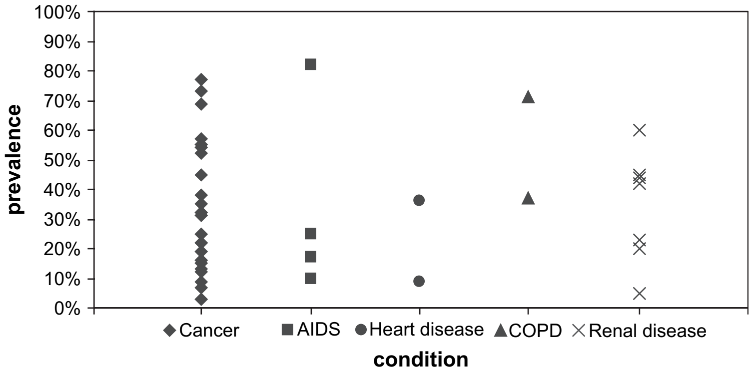

Fig. 1. Depression: Prevalences found in 33 studies for the five conditions. For most studies, a simple point prevalence was given. When studies reported a range (five studies), both maximum and minimum points in the range are shown.

if maximum prevalences are considered). In contrast, anxiety seemed to be less prevalent among AIDS patients (8%–34%) in comparison to the other four diseases (13%–79%).

Despite these variations within diseases, some patterns emerged. The results consistently show high prevalence for almost all considered symptoms. Most symptoms were found in one-third or more patients. Multiple symptoms occurred for all five diseases. However, two symptoms, pain and fatigue, were common in all five diseases, occurring in 34%–96% and 32%–90%, respectively. Breathlessness was common in most conditions, with a wide range of experience. However, it was most consistently found among patients with COPD and HD; the minimum values of prevalence was 90% and 60%, respectively, and the maximum values were prevalence was 95% and 88%, respectively. Insomnia was most common among AIDS patients (although this is based on only one study). Nausea was present in at least 43% of AIDS patients (compared with at least 6% of cancer patients, 17% of heart disease patients, and 30% of renal patients). Constipation seemed to be more frequent among cancer and renal patients (65% and 70%, respectively; maximum prevalence). Diarrhea was highly prevalent among AIDS patients, with a prevalence as high as 90%, against 29% in cancer, 12% in HD, and 21% in renal patients (though just single values were found for the latter two conditions). Anorexia was most common among cancer patients—present in up to 92% of the patients (against 41%, 67%, 64%, and 51% among HD, COPD, RD, and AIDS patients, respectively, though just a single value was found for the last).

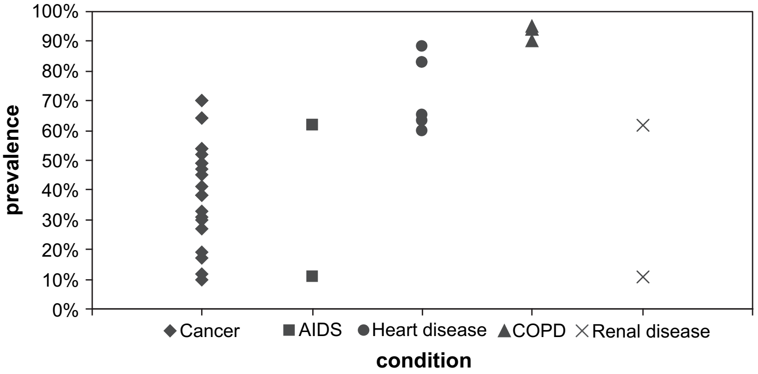

Fig. 2. Breathlessness: Prevalences found in 35 studies for the five conditions. For most studies, a simple point prevalence was given. When studies reported a range (three studies), both maximum and minimum points in the range are shown.

Table 2

Factors Contributing to the Variation in Symptom Prevalence: Depression as an Example

(A) Factors relating to the *definition* of the symptom[101,102]
  - Some authors defined depression as a symptom, others, as a subjective complaint (e.g., feeling depressed, in a low mood), others, as a psychiatric disorder as defined by DSM[103] or ICD[104] (e.g., major depression).
  - Some studies used the substitution criteria of Endicott,[105] e.g., replacing weight loss with depressive appearance in terminally ill patients, others did not.
  - Some authors raised the threshold during the assessment to allow for signs of depression, sadness, or low mood expected to be present in terminally ill patients, others did not.

(B) Factors relating to the *methods to detect "cases"* of depression[101,102]
  - Some studies refer to clinically recognized depression.
  - Some studies used single-item questionnaires to screen.
  - Some studies used screening questionnaires (e.g., HADS,[106] BDI[107]).
  - Some studies used diagnostic interviews (e.g., SADS,[108] SCID[109]).

(C) Factors relating to the *design*
  - Some authors sought point prevalence, others period prevalence (with a range of time periods), and others mixed both.[92]
  - Studies have different length of follow-up.

(D) Factors relating to the *sample*
  - Studies had varied sample sizes.
  - Studies included terminally ill patients at different stages of disease (e.g., according to predefined life expectancy, excluding patients who died after a predefined terminal phase period).

(E) Factors relating to the *setting of the study* and to the *accrual model*
  - Studies recruited patients from hospital wards, hospital acute wards, hospices, community-based units, outpatients clinics, etc.
  - Some studies attempted to avoid biased samples (e.g., patients from the mental health system, when assessing depression), others did not.

(F) Factors relating to the method of *data collection*
  - Some studies were based on recorded data (e.g., hospital records).
  - Some studies were based on recorded data about drugs prescribed (e.g., antidepressants).
  - Some studies interviewed the patient, others a carer, others a bereaved carer, and others interviewed staff members.

(G) Miscellaneous
  - Some studies only included symptoms if they had been severe and/or present according to a predefined frequency.
  - Some approaches accounted for the possibility of preexisting symptoms, others did not.
  - Some studies referred to new symptoms, others to symptoms as a result of treatment, others combined both.
  - Some studies did not recruit patients who were continuing curative treatment, others did.

Note: Superscripted numbers relate to the reference source.

Discussion

A first concern raised by this study is the wide range of symptom prevalences for individual diseases. This can be at least partially explained by the fact that studies differed regarding methodological procedures. Due to such heterogeneity, we felt it was not possible to aggregate the data using meta-analytic techniques. Therefore, we have displayed the results in terms of minimum and maximum prevalences. We identified eight clusters of different factors that contributed to this heterogeneity. First, there were factors relating to the definition of the symptom with different criteria and interpretation of the symptom across studies. Second, there were variations in the methods to detect cases of the symptom, with different questionnaires and screening methods used. Third, there were variations in study design, with a mix of point prevalence, period prevalence, and length of follow-up. Fourth, there were variations in the sample. In addition to variations in sample size, different authors defined the terminal or advanced stage of illnesses differently. Defining when a slowly progressive disease reaches advanced stages is difficult. Heart failure, renal failure, and especially AIDS have a fluctuating trajectory. This difficulty in prognostication may be one of the reasons why patients with noncancer conditions are not referred to palliative care services in some settings. Lack of a clear definition is also likely to have contributed to the variation in prevalence among both cancer and noncancer patients. Prognostic uncertainty suggests that palliative care should be made available on the basis of need, e.g., symptoms, rather than prognosis. Fifth, variation resulted from differences in study setting (hospital wards, hospice, community) and the method of recruitment and accrual. There were particular difficulties in some studies with biased samples—for example, patients with pain in pain clinics or patients from the mental health system when assessing mental depression. This fails to give a true population-based perspective. Six, there were variations in the methods of data collection. Some studies were based on recorded data, for example from routine hospital records; some directly interviewed patients' families. Other studies used proxies, either professionals or carers, and in some instances, bereaved carers. Probably least reliably, some studies relied on presence of symptoms by assessing whether drugs were prescribed or not. In particular, these studies may under-report the prevalence of symptoms. Seventh, some studies only included symptoms if they were severe or present according to predefined frequencies, whereas other studies included symptoms if they were simply present. Eighth, there was a great variety in the approaches to including patients with particular groups of symptoms. Some studies accounted for possible preexisting symptoms, some studies referred only to new symptoms, some studies looked at symptoms as a result of treatment but excluded preexisting symptoms, and some studies did not include patients who were continuing curative treatment.

In this study, we sought to compare symptom prevalence among people with five far advanced, life-limiting diseases. We did find eight comparative studies encompassing people in such conditions. However, three compared cancer with a mixed noncancer group (included several diseases),[11,18,19] two had few noncancer patients in the comparison,[20,21] and all compared no more than two conditions.[4,11,18–23] Thus, our comparisons had to be made between articles, limiting the comparability.

Nevertheless, our findings shed some light on what may constitute the core of the common pathway toward the end of life in terms of symptomatology. Three symptoms are particularly universal and frequent—pain, fatigue, and breathlessness—with prevalences often well above 50% in all five conditions. Insomnia and anorexia are also recurrent symptoms in all conditions. Despite their high prevalence, these symptoms face underassessment and undertreatment, each of which occurs for different reasons. This poses different challenges for the management of each symptom.

Methods of pain relief have improved considerably in the past two decades, especially for cancer-related pain.[24] Yet, there is evidence in some settings that pain control falls far short of the recommendations of the World Health Organization (WHO).[25] Wide dissemination and adoption of effective methods of pain control are required if pain relief is to be accessible to more people. Fatigue has not had the same scientific evolution as pain and effective treatments have not yet been identified. Underassessment is common, as this symptom is rarely discussed by physicians and patients,[26] although a consensus is emerging among patients, caregivers, and oncologists about the importance of fatigue in many progressive diseases.[27]

Breathlessness is also a difficult symptom to control with limited treatments.[28] Early intervention and teaching practical skills to patients and carers might be priorities given that this symptom tends to occur in acute episodes of crisis.[28,29] Although terminal patients with different conditions would benefit from better management of breathlessness, COPD patients are a particular group in need. Since insomnia is often caused by inadequate symptom control, attempts to optimize symptom control should be a priority in its treatment.[21] Because anorexia is not always an obvious condition, comprehensive and individualized routine screening is necessary.[30] There were some situations in which there were few data available, and research is needed to determine whether symptoms such as diarrhea are found among patients with COPD, advanced heart failure, or renal failure; nausea in COPD patients; and confusion in patients with advanced renal failure.

Our analysis showed that for patients with each of four diseases—AIDS, HD, COPD, and RD—11 symptoms are often as prevalent in advanced disease as among advanced cancer patients. Thus, there seems to be a common pathway that people with far advanced progressive diseases have to face. This suggests that palliative care is relevant for people with all five conditions, although aspects of assessment and management may need modification. Over the past decade, mutual cooperation among the WHO, governments, charitable initiatives, and palliative care policy makers has led to the recognition of need and subsequent inclusion of AIDS patients in palliative care services.[14] Cheap, effective, and culturally appropriate palliative care initiatives, such as the home-based palliative care program in Uganda, where palliative care is part of the national health plan, are to be pursued worldwide.[31,32] It would be a reasonable step forward to accurately plan how patients with other chronic, life-threatening illnesses, such as HD, COPD, and RD, could be embraced by such a benefit.

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References

1. World Health Organization. Active aging: A policy framework. Geneva: World Health Organization, 2002.

2. Davies E, Higginson IJ, eds. Palliative care: The solid facts. Milan: World Health Organization Regional Office for Europe, 2004.

3. Davies E, Higginson IJ, eds. Better palliative care for older people: The solid facts. Milan: World Health Organization Regional Office for Europe, 2004.

4. Edmonds P, Karlsen S, Khan S, Addington-Hall JM. A comparison of the palliative care needs of patients dying from chronic respiratory disease and lung cancer. Palliat Med 2001;15: 287–295.

5. Higginson IJ, Jarman B, Astin P, Dolan S. Do social factors affect where patients die: an analysis of 10 years of cancer deaths in England. J Public Health 1999;21(1):22–28.

6. Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: global burden of disease study. Lancet 1997;349(9061):1269–1276.

7. Cartwright A. Changes in life and care in the year before death 1969–1987. J Public Health Med 1991;13(2):81–87.

8. Anderson H, Ward C, Eardley A, et al. The concerns of patients under palliative care and a heart failure clinic are not being met. Palliat Med 2001; 15:279–286.

9. Gibbs LME, Addington-Hall J, Gibbs JS. Dying from heart failure: lessons from palliative care. BMJ 1998;317(7164):961–962.

10. Higginson IJ. Palliative care: a review of past changes and future trends. J Public Health Med 1993;15:3–8.

11. Tranmer JE, Heyland D, Dudgeon D, et al. Measuring the symptom experience of seriously ill cancer and noncancer hospitalized patients near the end of life with the Memorial Symptom Assessment Scale. J Pain Symptom Manage 2003;25(5): 420–429.

12. Butters E, Higginson IJ. Two HIV/AIDS community support teams: patient characteristics, problems at referral and during the last 6 weeks of life. AIDS Care 1995;7(5):593–603.

13. Gore JM, Brophy CJ, Greenstone MA. How well do we care for patients with end stage chronic obstructive pulmonary disease (COPD)? A comparison of palliative care and quality of life in COPD and lung cancer. Thorax 2000;55(12):1000–1006.

14. Sepulveda C, Marlin A, Yoshida T, Ullrich A. Palliative care: the World Health Organization's global perspective. J Pain Symptom Manage 2002; 24(2):91–96.

15. Hinton J. The physical and mental stress of dying. Q J Med 1963;32:1–21.

16. O'Brien T, Welsh J, Dunn FG. ABC of palliative care: non-malignant conditions. BMJ 1998; 316(7127):286–289.

17. Addington-Hall J, Higginson IJ, eds. Palliative care for non-cancer patients, 1st ed. New York: Oxford University Press, 2001.

18. Addington-Hall JM, Fakhoury W, McCarthy M. Specialist palliative care in non-malignant disease. Palliat Med 1998;12:417–427.

19. Addington-Hall JM, McCarthy M. Dying from cancer: results of a national population-based investigation. Palliat Med 1995;9:295–305.

20. Durkin I, Kearney M, O'Siorain L. Psychiatric disorder in a palliative care unit. Palliat Med 2003; 17:212–218.

21. Hugel H, Ellershaw JE, Cook L, Skinner J, Irvine C. The prevalence, key causes and management of insomnia in palliative care patients. J Pain Symptom Manage 2004;27(4):316–321.

22. Lynn J, Teno JM, Phillips RS, et al. Perceptions by family members of the dying experience of older and seriously ill patients. Ann Intern Med 1997; 126(2):97–106.

23. Murray SA, Boyd K, Kendall M, et al. Dying of lung cancer or cardiac failure: prospective qualitative interview study of patients and their carers in the community. BMJ 2002;325(7370):929–932.

24. Portenoy RK. Cancer-related fatigue: an immense problem. Oncologist 2000;5(5):350–352.

25. Bernabei R, Gambassi G, Lapane K, et al. Management of pain in elderly patients with cancer. JAMA 1998;279(23):1877–1882.

26. Vogelzang NJ, Breitbart W, Cella D, et al. Patient, caregiver, and oncologist perceptions of cancer-related fatigue: results of a tripart assessment survey. The Fatigue Coalition. Semin Hematol 1997;34(3 Suppl 2):4–12.

27. Curt GA. Fatigue in cancer. BMJ 2001; 322(7302):1560.

28. Andrewes T. The management of breathlessness in palliative care. Nurs Stand 2002;17(5):43–52.

29. Higginson I, McCarthy M. Measuring symptoms in terminal cancer: are pain and dyspnoea controlled? J R Soc Med 1989;82(5):264–267.

30. Strasser F, Bruera ED. Update on anorexia and cachexia. Hematol Oncol Clin North Am 2002; 16(3):589–617.

31. The untapped potential of palliative care for AIDS. Lancet 2003;362(9398):1773.

32. Ramsay S. Leading the way in African home–based palliative care. Free oral morphine has allowed expansion of model home-based palliative care in Uganda. Lancet 2003;362(9398):1812–1813.

33. Addington-Hall JM, MacDonald M, Anderson H, Freeling P. Dying from cancer: the views of bereaved family and friends about the experiences of terminally ill patients. Palliat Med 1991;5:207–214.

34. Addington-Hall JM. Heart disease and stroke: lessons from cancer care. In: Ford G, Lewin I, eds. Managing terminal illness. London: Royal College of Physicians, 1996.

35. Bruera E. Research in symptoms other than pain. In: Doyle D, Hanks GW, MacDonald M, eds. The Oxford textbook of palliative medicine. New York: Oxford University Press, 1998: 179–185.

36. Chow E, Fung K, Panzarella T, et al. A predictive model for survival in metastatic cancer patients attending an outpatient palliative radiotherapy clinic. Int J Radiat Oncol Biol Phys 2002;53(5): 1291–1302.

37. Cleeland CS, Gonin R, Hatfield AK, et al. Pain and its treatment in outpatients with metastatic cancer. N Engl J Med 1994;330(9):592–596.

38. Hearn J, Higginson IJ. Cancer pain epidemiology: a systematic review. In: Bruera ED, Portenoy RK, eds. Cancer pain: Assessment and management. London: Cambridge University Press, 2003: 19–37.

39. Meuser T, Pietruck C, Radbruch L, et al. Symptoms during cancer pain treatment following WHO-guidelines: a longitudinal follow-up study of symptom prevalence, severity and etiology. Pain 2001;93(3):247–257.

40. Morita T, Tsunoda J, Inoue S, Chihara S. Contributing factors to physical symptoms in terminally-ill cancer patients. J Pain Symptom Manage 1999;18(5):338–346.

41. Potter J, Hami F, Bryan T, Quigley C. Symptoms in 400 patients referred to palliative care services: prevalence and patterns. Palliat Med 2003;17:310–314.

42. Vainio A, Auvinen A. Prevalence of symptoms among patients with advanced cancer: an international collaborative study. J Pain Symptom Manage 1996;12(1):3–10.

43. Dunlop GM. A study of the relative frequency and importance of gastrointestinal symptoms and weakness in patients with far advanced cancer. Palliat Med 1989;4:37–43.

44. Reuben DB, Mor V, Hiris J. Clinical symptoms and length of survival in patients with terminal cancer. Arch Intern Med 1988;148(7):1586–1591.

45. Curtis EB, Krech R, Walsh TD. Common symptoms in patients with advanced cancer. J Palliat Care 1991;7(2):25–29.

46. Brescia FJ, Adler D, Gray G, et al. Hospitalized advanced cancer patients: a profile. J Pain Symptom Manage 1990;5(4):221–227.

47. Ventafridda V, De Conno F, Ripamonti C, Gamba A, Tamburini M. Quality-of-life assessment during a palliative care programme [see comment]. Ann Oncol 1990;1(6):415–420.

48. Breitbart W, McDonald MV, Rosenfeld B, et al. Pain in ambulatory AIDS patients. I: Pain characteristics and medical correlates. Pain 1996;68(2–3): 315–321.

49. Singer EJ, Zorilla C, Fahy-Chandon B, et al. Painful symptoms reported by ambulatory HIV-infected men in a longitudinal study. Pain 1993; 54(1):15–19.

50. Vogl D, Rosenfeld B, Breitbart W, et al. Symptom prevalence, characteristics, and distress in AIDS outpatients. J Pain Symptom Manage 1999;18(4): 253–262.

51. Levenson JW, McCarthy EP, Lynn J, Davis RB, Phillips RS. The last six months of life for patients with congestive heart failure. J Am Geriatr Soc 2000;48(Suppl):101–109.

52. Nordgren L, Sorensen S. Symptoms experienced in the last six months of life in patients with end-stage heart failure. Eur J Cardiovasc Nurs 2003; 2(3):213–217.

53. Skilbeck J, Mott L, Page H, et al. Palliative care in chronic obstructive airways disease: a needs assessment. Palliat Med 1998;12:245–254.

54. Davison S. Pain in hemodialysis patients: prevalence, cause, severity, and management. Am J Kidney Dis 2003;42(6):1239–1247.

55. Kimmel P, Emont S, Newmann J, Danko H, Moss A. ESRD patient quality of life: symptoms, spiritual beliefs, psychosocial factors, and ethnicity. Am J Kidney Dis 2003;42(4):713–721.

56. Akechi T, Okuyama T, Sugawara Y, et al. Major depression, adjustment disorders, and post-traumatic stress disorder in terminally ill cancer patients:

associated and predictive factors. J Clin Oncol 2004; 22(10):1957–1965.

57. Breitbart W, Jaramillo JR, Chochinov HMC. Palliative and terminal care. In: Holland JC, ed. Psycho-oncology. New York: Oxford University Press, 1998: 437–449.

58. Hagerty RG, Butow PN, Ellis PA, et al. Cancer patient preferences for communication of prognosis in the metastatic setting. J Clin Oncol 2004; 22(9):1721–1730.

59. Lloyd-Williams M, Friedman T, Rudd N. Criterion validation of the Edinburgh postnatal depression scale as a screening tool for depression in patients with advanced metastatic cancer. J Pain Symptom Manage 2000;20(4):259–265.

60. Minagawa H, Uchitomi Y, Yamawaki S, Ishitani K. Psychiatric morbidity in terminally ill cancer patients: a prospective study. Cancer 1996; 78(5):1131–1137.

61. Regnard C, Hockley J. A guide to symptom relief in palliative care. Abingdon: Radcliffe Medical Press, 2004.

62. Smith EM, Gomm SA, Dickens CM. Assessing the independent contribution to quality of life from anxiety and depression in patients with advanced cancer. Palliat Med 2003;17:509–513.

63. Stone P, Hardy J, Broadley K, et al. Fatigue in advanced cancer: a prospective controlled cross-sectional study. Br J Cancer 1999;79(9/10):1479–1486.

64. Rabkin JG, Ferrando SJ, Jacobsberg LB, Fishman B. Prevalence of axis I disorders in an AIDS cohort: a cross-sectional, controlled study. Compr Psychiatry 1997;38(3):146–154.

65. Tross S, Hirsch DA. Psychological distress and neuropsychological complications of HIV infection and AIDS. Am Psychol 1988;43(11):929–934.

66. Gibbs JSR. Heart disease. In: Addington-Hall J, Higginson IJ, eds. Palliative care for non-cancer patients. New York: Oxford University Press, 2001: 30–43.

67. Levy J, Morgan J, Brown E. Oxford handbook of dialysis. New York: Oxford University Press, 2001.

68. Martin CR, Thompson DR. Prediction of quality of life in patients with end-stage renal disease. Br J Health Psychol 2000;5:41–55.

69. Walters B, Hays R, Spritzer K, Fridman M, Carter W. Health-related quality of life, depressive symptoms, anemia, and malnutrition at hemodialysis initiation. Am J Kidney Dis 2002;40(6): 1185–1194.

70. Watnick S, Kirwin P, Mahnensmith R, Concato J. The prevalence and treatment of depression among patients starting dialysis. Am J Kidney Dis 2003;41(1):105–110.

71. Weisbord SD, Carmody SS, Bruns FJ, et al. Symptom burden, quality of life, advance care planning and the potential value of palliative care in severely ill haemodialysis patients. Nephrol Dial Transplant 2003;18(7):1345–1352.

72. Wuerth D, Finkelstein SH, Kliger AS, Finkelstein FO. Chronic peritoneal dialysis patients diagnosed with clinical depression: results of pharmacologic therapy. Semin Dial 2003;16(6):424–427.

73. Butters E, George R, Higginson IJ. Audit methods: HIV/AIDS care. In: Higginson IJ, ed. Clinical audit in palliative care. Abingdon: Radcliffe Medical Press, 1995: 101–112.

74. Claessens MT, Lynn J, Zhong Z, et al. Dying with lung cancer or chronic obstructive respiratory disease: insights from SUPPORT. J Am Geriatr Soc 2000;48(Suppl):S146–S153.

75. Gysels M, Higginson IJ, eds. Improving supportive and palliative care for adults with cancer. CD-ROM. London: National Institute for Clinical Excellence, 2004.

76. Breitbart W, Chochinov H, Passik S. Psychiatric symptoms in palliative medicine. In: Derek D, Hanks G, Cherny N, Calman K, eds. Oxford textbook of palliative medicine. New York: Oxford University Press, 2004: 746–771.

77. Bruera E, Miller L, McCallion J, et al. Cognitive failure in patients with terminal cancer: a prospective study. J Pain Symptom Manage 1992;7(4): 192–195.

78. Caraceni A, Nanni O, Maltoni M, et al. Impact of delirium on the short term prognosis of advanced cancer patients. Cancer 2000;89(5): 1145–1149.

79. Cobb JL, Glantz MJ, Nicholas PK, et al. Delirium in patients with cancer at the end of life. Cancer Pract 2000;8(4):172–177.

80. Gagnon P, Allard P, Masse B, DeSerres M. Delirium in terminal cancer: a prospective study using daily screening, early diagnosis, and continuous monitoring. J Pain Symptom Manage 2000;19(6): 412–426.

81. Lawlor PG, Gagnon B, Mancini IL, et al. Occurrence, causes, and outcome of delirium in patients with advanced cancer. Arch Intern Med 2000;160(6):786–794.

82. Jones K, Breitbart W. Palliative care research in human immunodeficiency virus/acquired immunodeficiency syndrome: clinical trials of symptomatic therapies. In: Portenoy RK, Bruera E, eds. Issues in palliative care. New York: Oxford University Press, 2003: 371–401.

83. Neuenschwander H, Bruera E. Asthenia. In: Doyle D, Hanks GWC, MacDonald M, eds. Oxford textbook of palliative medicine. New York: Oxford University Press, 1998: 573–581.

84. Breitbart W, McDonald MV, Rosenfeld B, Monkman ND, Passik S. Fatigue in ambulatory AIDS patients. J Pain Symptom Manage 1998;15(3): 159–167.

85. Parfrey PS, Vavasour HM, Henry S, Bullock M, Gault MH. Clinical features and severity of nonspecific symptoms in dialysis patients. Nephrology 1988;50:121–128.

86. Dudgeon D. Multidimensional assessment of dyspnea. In: Portenoy RK, Bruera E, eds. Issues in palliative care research. New York: Oxford University Press, 2003: 83–96.

87. Dudgeon DJ, Kristjanson L, Sloan JA, Lertzman M, Clement K. Dyspnea in cancer patients: prevalence and associated factors. J Pain Symptom Manage 2001;21(2):95–102.

88. Ross DD, Alexander CS. Management of common symptoms in terminally ill patients: part II. Constipation, delirium and dyspnea. Am Fam Physician 2001;64(6):1019–1026.

89. Loos C, Briancon S, Frimat L, Hanesse B, Kessler M. Effect of end-stage renal disease on the quality of life of older patients. J Am Geriatr Soc 2003;51(2):229–233.

90. Iliescu EA, Coo H, McMurray MH, et al. Quality of sleep and health-related quality of life in haemodialysis patients. Nephrol Dial Transplant 2003; 18(1):126–132.

91. Bruera E, Seifert L, Watanabe S, et al. Chronic nausea in advanced cancer patients: a retrospective assessment of a metoclopramide-based antiemetic regimen. J Pain Symptom Manage 1996;11(3): 147–153.

92. Potter J, Higginson I. Frequency and severity of gastrointestinal symptoms in advanced cancer. In: Ripamonti C, Bruera E, eds. Gastrointestinal symptoms in advanced cancer. London: Oxford University Press, 2002: 1–15.

93. Sarhill N, Mahmoud F, Walsh D, et al. Evaluation of nutritional status in advanced metastatic cancer. Support Care Cancer 2003;11(10):652–659.

94. Radin Kimball L, McCormick WC. The pharmacologic management of pain and discomport in persons with AIDS near the end of life: use of opioid analgesia in the hospice setting. J Pain Symptom Manage 1996;11(2):88–94.

95. McCann K, Boore JRP. Fatigue in persons with renal failure who require maintenance haemodialysis. J Adv Nurs 2000;32(5):1132–1142.

96. Merkus M, Jager K, Dekker F, et al. Physical symptoms and quality of life in patients on chronic dialysis: results of The Netherlands cooperative study on adequacy of dialysis (NECOSAD). Nephrol Dial Transplant 1999;14(5):1163–1170.

97. Yasuda G, Shibata K, Takizawa T, et al. Prevalence of constipation in continuous ambulatory peritoneal dialysis patients and comparison with hemodialysis patients. Am J Kidney Dis 2002;39(6): 1292–1299.

98. Mercadante S. Diarrhea in terminally ill patients: pathophysiology and treatment. J Pain Symptom Manage 1995;10(4):298–309.

99. Meyer M. Palliative care and AIDS: 2. Gastrointestinal symptoms. Int J STD AIDS 1999;10(8): 495–505.

100. Hawkins C. Anorexia and anxiety in advanced malignancy: the relative problem. J Hum Nutr Diet 2000;13(2):113–117.

101. Hotopf M, Chidgey J, Addington-Hall JM, Ly KL. Depression in advanced disease: a systematic review. Part 1: prevalence and case finding. Palliat Med 2002;16:81–97.

102. Breitbart W, Bruera E, Chochinov H, Lynch M. Neuropsychiatric syndromes and psychological symptoms in patients with advanced cancer. J Pain Symptom Manage 1995;10(2):131–141.

103. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC: American Psychiatric Association, 1994.

104. World Health Organization. The tenth revision of the International Classification of Diseases and Related Health Problems (ICD-10). Geneva: World Health Organization, 1992.

105. Endicott J. Measurement of depression in patients with cancer. Cancer 1984;53(Suppl): 2243–2248.

106. Zigmond A, Snaith R. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983; 67:361–370.

107. Beck A, Ward C, Mendelson M. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561–571.

108. Endicott J, Spitzer A. A diagnostic interview: the schedule for affective disorders and schizophrenia. Arch Gen Psychiatry 1978;35:773–782.

109. Spitzer A, Williams J, Gibbon M, First M. The Structured Clinical Interview for DSM-III-R (SCID): 1. History, rationale, and description. Arch Gen Psychiatry 1992;49:624–629.

Appendix
List of Texts Included in Search

Addington-Hall J, Higginson IJ, eds. Palliative care for non-cancer patients. New York: Oxford University Press, 2001.

Bruera E, Portenoy RK, eds. Cancer pain: Assessment and management. Cambridge: Cambridge University Press, 2003.

Chochinov HM, Breitbart W, eds. Handbook of psychiatry in palliative medicine. Oxford: Oxford University Press, 2000.

Doyle D, Hanks GWC, MacDonald M, eds. Oxford textbook of palliative medicine. Oxford: Oxford University Press, 2004.

Doyle D, Hanks GWC, MacDonald M, eds Oxford textbook of palliative medicine. Oxford: Oxford University Press, 1998.

Ford G, Lewin I, eds. Managing terminal illness. London: Royal College of Physicians of London, 1996.

Higginson IJ, ed. Clinical audit in palliative care. Abingdon: Radcliffe Medical Press, 1993.

Hoskin P, Makin W, eds. Oncology for palliative medicine. New York: Oxford University Press, 1998.

Joishy SK, ed. Palliative medicine secrets. Philadelphia: Hanley & Belfus, 1999.

Levy J, Morgan J, Brown E. Oxford handbook of dialysis. New York: Oxford University Press, 2001.

Portenoy RK, Bruera E, eds. Issues in palliative care research. Oxford: Oxford University Press, 2003.

Regnard C, Hockley J. A guide to symptom relief in palliative care. Abingdon: Radcliffe Medical Press, 2004.

Ripamonti C, Bruera E, eds. Gastrointestinal symptoms in advanced cancer patients. Oxford: Oxford University Press, 2002.