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# Daily symptom burden in end-stage chronic organ failure: a systematic review

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Chronic diseases are nowadays the major cause of morbidity and mortality worldwide. Patients with end-stage chronic organ failure may suffer daily from distressful physical and psychological symptoms. The objective of the present study is to systematically review studies that examined daily symptom prevalence in patients with end-stage chronic organ failure, with attention to those that included patients with either congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD) or chronic renal failure (CRF). Thirty-nine articles (8 CHF, 7 COPD, 2 CHF and COPD, 22 CRF) have been included. The included studies used various study designs. There was a wide range of daily symptom prevalence that may be due to the heterogeneity in methodology used. Nevertheless, findings suggest significant symptom burden in these patients. This review highlights the need for further prospective and longitudinal research on symptom prevalence in patients with end-stage CHF, COPD and CRF to facilitate the development of patient-centred palliative care programs. *Palliative Medicine* (2008); **22**: 938–948

**Key words:** chronic obstructive pulmonary disease; congestive heart failure; chronic kidney failure; palliative care; symptom burden

## Introduction

Chronic diseases are presently a major cause of morbidity and mortality worldwide.[1] The prevalence of congestive heart failure (CHF),[2] chronic obstructive pulmonary disease (COPD)[3] and chronic renal failure (CRF)[4] is expected to rise over the next years. The prognosis of survival for patients with chronic organ failure is even poorer than that for many common malignant diseases.[5,6]

To date, several authors have suggested that palliative care may have an important role in chronic non-malignant diseases.[5–8] Indeed, previous research has shown that both patients with end-stage malignant and non-malignant diseases may suffer from many distressful physical and psychological symptoms such as fatigue, pain, dyspnoea, cough, lack of appetite, sadness and sleep disorders.[9] Moreover, previous studies have shown that quality of life in patients with CHF, COPD or CRF is equally or even more greatly affected by their disease than those with cancer.[6,10,11] However, until now palliative care has been reserved mostly for patients with malignant disease as evidenced by the limited access to palliative care for patients with non-malignant disease.[12] Even with the increasing recognition of the need for palliative care for these patients, current clinical guidelines on the management of chronic disease offer little guidance on end-of-life care issues[13,14] and care for patients with end-stage disease is presently prioritised by diagnosis rather than need.[15] The disparity in care, despite evidence to the contrary, likely reflects the uncertainty in the prognosis in terms of survival in patients with chronic organ failure.[7,16] The course of end-stage chronic organ failure is marked typically by a gradual decrease and punctuated by acute deteriorations in health status and daily functioning, especially in COPD and CHF.[17] These deteriorations can be life threatening and increase the risk of hospital admission and intensive treatment.[18] Thus, although there is a gradual decrease in health status and daily functioning in patients with CHF, COPD or CRF,[17] timing of death remains uncertain and choosing the right moment for starting palliative care is a continuous challenge for the treating physician.[19] Essential to any patient-centred palliative care program is an understanding of the self-perceived daily symptoms of patients with end-stage CHF, COPD or CRF.[20]

In the present systematic review, we have critically appraised the currently available peer-reviewed literature that addresses daily symptom burden of patients with CHF, COPD or CRF at the end of their life.

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## Methods

### Data sources and searches

A computerised literature search was performed to identify relevant articles. Several databases were used: MEDLINE/PubMed (timespan: 1966 to April 2007) and Web of Science (timespan: 1988 to April 2007) with the following three groups of keywords:

1) COPD, pulmonary disease chronic obstructive, end-stage lung failure, end-stage lung disease, heart failure congestive, end-stage heart disease, kidney failure chronic, dialysis, end-stage renal disease;
2) palliative care, hospice care, terminal care, terminally ill, end-of-life;
3) symptoms, pain, dyspnoea, breathlessness, cough, fatigue, anorexia, weight loss, depression, anxiety, delirium, confusion, insomnia, oedema, dizziness, nausea, mouth problems, pruritus, constipation.

The three groups were combined using '*and*'. Within each group the keywords were combined using '*or*'. In addition, reference lists of original articles were searched by hand to identify articles that may contain information on the topic of interest and may have been missed by the search strategy. Finally, corresponding authors of articles were contacted at least twice in an effort to include all available studies.

### Study selection

Articles were included that reported original data on daily symptoms in adult patients with CHF, COPD or CRF at the end of their life and if the presence of one or more of the aforementioned symptoms in patients with CHF, COPD or CRF at the end of their life was reported in the abstract. Articles not written in English were excluded. The authors included observational studies with various study designs, such as cross-sectional, longitudinal, retrospectively and/or prospectively. Abstracts, reviews, editorials, qualitative studies and case reports were considered ineligible.

### Data extraction and quality assessment

Two reviewers (D.J.A.J. and M.A.S.) assessed the methodological quality of the included studies. A predesigned data extraction form was used to obtain data on study design and relevant results. For each study, authors, journal, year of publication, country of origin and studied disease(s) were recorded. For quality assessment, studies were evaluated on the following items: design of the study (prospective or retrospective, cross-sectional or longitudinal, patient reporting, proxy reporting or chart review), number of patients, response rate and patient characteristics (severity of the disease, prognosis, age, gender, setting). For each of the symptoms, the definition of the symptom, method of measurement (if reported) and the reported prevalence was noted. Finally, the limitations of each study were considered.

### Data synthesis and analysis

The use of meta-analytic techniques for data-analysis was not possible, because of variability of design, patient characteristics, and definition and measurement of symptoms that were used. Therefore, for each symptom, minimum, maximum and median prevalence numbers are reported for each chronic disease. Prevalence numbers are reported for patients who were not identified as terminally ill and patients who were, often retrospectively, identified as terminally ill, for example, the last 2 weeks of life, the last week of life, the last 3 days of life or the last 24 h of life. For CRF, discontinuation or declining of dialysis was also terminal illness defining event.

## Results

In total, 595 articles were identified in the electronic searches, 515 were written in English. Of these articles, 79 were considered eligible after reading the abstract. Five case studies, letters and editorials, seven qualitative studies and 27 reviews were excluded. In addition, 14 articles were selected from reference lists of the remaining 40 articles. In total, 54 articles were reviewed in detail. Six articles were excluded because prevalence numbers were only reported for a combined group of diseases (e.g., CHF, COPD and liver disease) and three studies because symptom prevalence numbers were not mentioned. Six studies were excluded for other reasons. In total, 39 articles were considered eligible. Eight studies included patients with end-stage CHF, seven included patients with end-stage COPD, two included both patients with end-stage CHF and patients with end-stage COPD and 22 studies included patients with end-stage CRF (Figure 1).

A cross-sectional design was used in 32 studies and a longitudinal design in 7 studies. Thirteen studies were retrospective, mostly bereavement studies, and 23 were prospective. Retrospective and prospective information was combined in three studies. Patient reporting was used in 19 studies, proxy reporting in 10 studies, chart review in four studies and six studies combined patient and proxy reporting or chart review (Table 1).

Severity of the disease and prognosis of survival varied and was sometimes unknown. Therefore, the estimated prognosis for survival and, if this was unknown, the description of disease severity have been reported in Table 1. CHF patients with New York Heart Association (NYHA) class III or IV were included.[21–23] In the studies

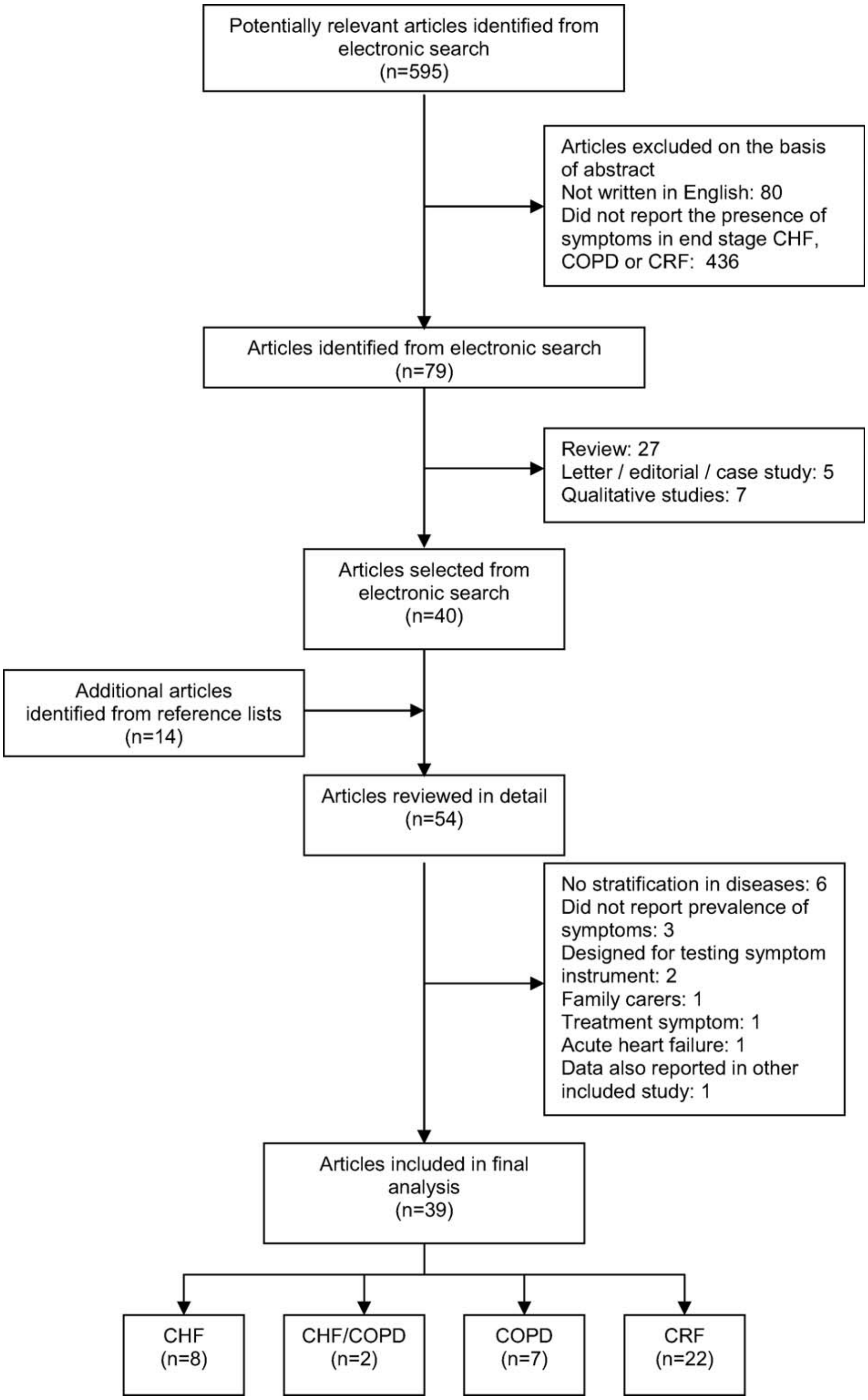

**Figure 1** Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure.

that included patients with COPD, forced expiratory volume in the first second ($FEV_1$) was only reported in two studies (mean $FEV_1$: 34% of predicted[24]; median $FEV_1$ 26.3% of predicted).[25] All CRF studies included patients who needed dialysis or became terminal after discontinuation or declining of dialysis. When reported, estimated prognosis of survival ranged from 24 h to 1 year.

Reported mean age ranged from 67 to 86 years (CHF); 65 to 75 years (CHF/COPD); 67 to 77 years (COPD) and 38 to 85 years (CRF). In the studies included in this sys-

**Table 1** Design of the included studies and (estimated) prognosis of survival or disease severity

| Disease | Design of the study | | | (Estimated) prognosis of survival or disease severity of patients |
|---|---|---|---|---|
| CHF, $n = 8$ | Longitudinal, $n = 3$ | Retrospective, $n = 3$ | Proxy reporting, $n = 2$ | Last 3 days, $n = 1$[22]<br>Last 2 weeks, $n = 1$[32] |
| | | | Chart review, $n = 1$ | Last 6 months, $n = 1$[40] |
| | Cross-sectional, $n = 5$ | Prospective, $n = 2$ | Patient reporting, $n = 2$ | End-stage, $n = 1$[59]<br><6 months, $n = 1$[60] |
| | | Retrospective, $n = 3$ | Proxy reporting, $n = 2$ | Last 24 hours, $n = 1$[23]<br>Last year/last week, $n = 1$[31] |
| | | | Chart review, $n = 1$ | <3 months/last week, $n = 1$[39] |
| CHF/COPD, $n = 2$ | Cross-sectional, $n = 2$ | Prospective, $n = 1$ | Patient reporting, $n = 1$ | Advanced disease, $n = 1$[21] |
| | | Retrospective, $n = 1$ | Proxy reporting, $n = 1$ | Last 3 days, $n = 1$[28] |
| COPD, $n = 7$ | Longitudinal, $n = 1$ | Prospective and retrospective, $n = 1$ | Patient/proxy reporting, $n = 1$ | <1 year, $n = 1$[45] |
| | Cross-sectional, $n = 6$ | Prospective, $n = 4$ | Patient reporting, $n = 3$ | Severe, $n = 2$[24,25]<br>End-stage, $n = 1$[61] |
| | | | Patient/proxy reporting, $n = 1$ | Severe, $n = 1$[44] |
| | | Retrospective, $n = 2$ | Proxy reporting, $n = 2$ | Last year/last week, $n = 1$[29]<br>Last year, $n = 1$[30] |
| CRF, $n = 22$ | Longitudinal, $n = 3$ | Retrospective, $n = 1$ | Chart review, $n = 1$ | Terminal after discontinuation of dialysis, $n = 1$[42] |
| | | Prospective and retrospective, $n = 2$ | Proxy reporting, $n = 1$ | Terminal after discontinuation of dialysis, $n = 1$[34] |
| | | | Patient/proxy/chart reporting, $n = 1$ | Terminal after discontinuation of dialysis, $n = 1$[48] |
| | Cross-sectional, $n = 19$ | Prospective, $n = 16$ | Patient reporting, $n = 13$ | End-stage, requiring dialysis, $n = 13$[8,10,47,50,51,53–55,62–66] |
| | | | Patient/proxy/chart reporting, $n = 3$ | Terminal after discontinuation of dialysis, $n = 1$[52]<br>End-stage, requiring dialysis, $n = 2$[49,67] |
| | | Retrospective, $n = 3$ | Proxy reporting, $n = 2$ | Last week, $n = 1$[33]<br>Terminal, $n = 1$[68] |
| | | | Chart review, $n = 1$ | Last 24 h, $n = 1$[41] |

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure.

tematic review, response rate of patients with CHF, COPD and CRF ranged from 40% to 100%. Although response rate was often not reported and if reported varied in definition, it did not seem to relate to certain diseases or study designs.

For measurement of most of the symptoms, different study designs were used. This is shown for the frequently reported daily symptoms fatigue, dyspnoea, pain and insomnia (Figure 2).

Despite the fact that there is a wide range in the reported prevalence of symptoms, some patterns are apparent (Table 2). Patients with CHF, COPD and CRF are likely to experience a high daily symptom burden, with fatigue being the most common symptom. Dyspnoea, insomnia and pain are frequently reported in all three diseases (Figure 3).

## Discussion

The present systematic review of observational studies of symptom prevalence in chronic organ failure shows that there is great heterogeneity in study designs used for studying symptoms in end-stage CHF, COPD and CRF. Daily symptom burden is likely to be high in end-stage chronic organ failure, irrespective of the underlying disease. However, to our knowledge, a comparison of symptom prevalence between patients with CHF, COPD and CRF at the end of life has not been made. The most frequently reported symptoms in CHF, COPD and CRF were fatigue, dyspnoea, insomnia and pain. As many of the symptoms were not included in studies of patients who were terminally ill, a comparison of symptomonology of the terminally ill with those who were not was not possible.

Our findings are in line with the findings of Solano, *et al.*[26] systematic review of symptom prevalence in far advanced cancer, AIDS, CHF, COPD and CRF. They also found a great heterogeneity in prevalence of symptoms and a high rate of prevalence for almost all symptoms. Pain, breathlessness and fatigue were the most common reported symptoms in the diseases they reviewed.[26] A recent systematic review of symptoms in end-stage CRF also found a wide variation in the prevalence of symptoms although the overall symptom burden seemed to be high, comparable with the findings in the present study.[27]

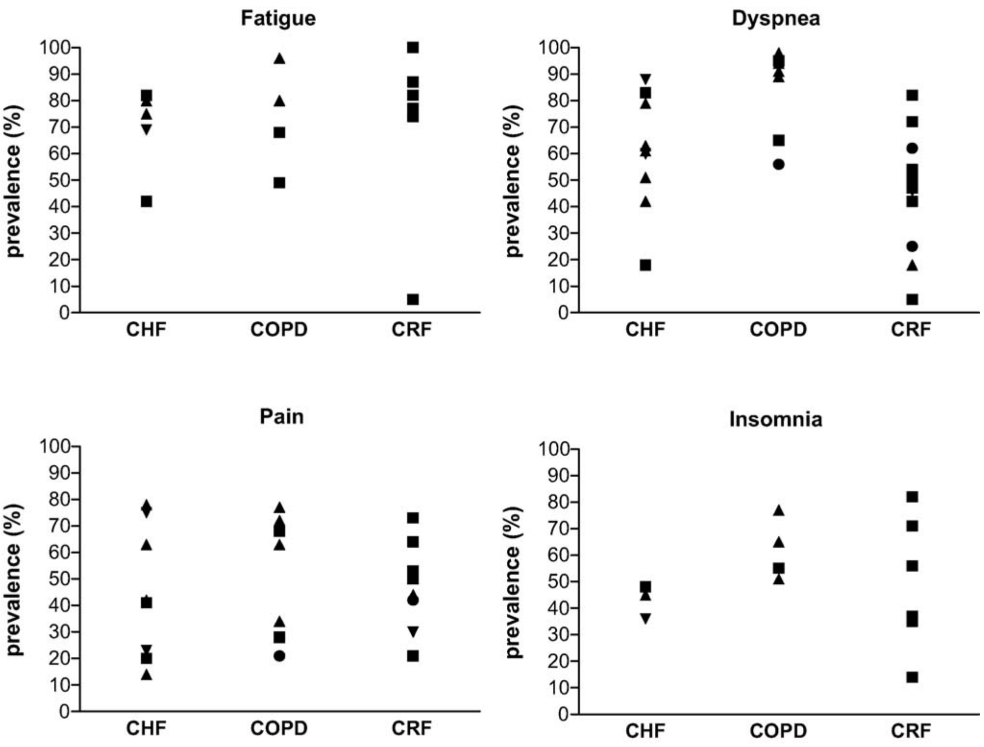

**Figure 2** Study design and prevalence of the reported symptoms fatigue (left upper quadrant), dyspnoea (right upper quadrant), pain (left lower quadrant) and insomnia (right lower quadrant) in patients with end-stage congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD) or chronic renal failure (CRF). ■, prospective patient reporting; ▲, retrospective proxy reporting; ▼, chart review; •, mixed patient or proxy reporting and retrospective or prospective.

## Limitations and methodological considerations

Because it is difficult to accurately determine the prognosis for survival in patients with end-stage CHF, COPD or CRF, authors who used prospective study designs may not have identified their patients as being at the end of life. Therefore, our search strategy may have failed to identify some relevant articles. Furthermore, some authors focused on a limited number of symptoms, and thereby our review may be underreporting some of the less commonly examined symptoms.

The variability in symptom prevalence we observed is likely the result of the heterogeneity in study design. Therefore, four causes probably contributing to the great variability will be discussed.

First, in this systematic review, studies of various designs, such as cross-sectional, longitudinal, retrospectively and/or prospectively, patient reporting, proxy reporting and chart review have been included. The reported symptom prevalence could probably be influenced by the design of the study. For example, some of the studies included in this systematic review relied on bereaved family members to act as proxies to report on the daily symptoms experienced by the patient.[22,23,28–34] These proxies included relatives (partners and children),[22,23,28–34] friends,[29,31,32] neighbours[29,31] or professional caregivers.[29,31] In general, proxy respondent agreement on health symptoms is better for proxies living with the patient compared with proxies not living with the patient. Children of patients have been shown to report more symptoms than partners of patients. Caregivers, like physicians, may report depression less frequently than relatives.[35] This is true not only for depression but also for pain, anxiety and other symptoms bereaved family members and medical staff have shown poor agreement.[36] Previous research in patients with cancer and their relatives has shown a low agreement between family members' ratings and the patients' own ratings of their experienced symptoms.[37] The low and inconsistent agreement brings into question the use of family members' or professional caregivers' views as proxies for the views of patients. Whether the study is prospective or retrospective can also have an impact. In retrospective assessment of symptoms, family members rate problems as mild or severe and avoid the mid-points of a rating scale, in contrast to what is seen in prospective assessment.[36]

Timing of the interview is an important consideration in post-bereavement studies because passage of time may change the perception of daily symptom burden by relatives. Studies included in this review conducted interviews within 1 month,[23] within 5–10 months[30] or until 10 months after death.[31] It has been shown that pain and

**Table 2** Symptom prevalence

| Symptom | CHF | CHF terminal | COPD | COPD terminal | CRF | CRF terminal |
|---|---|---|---|---|---|---|
| Fatigue | 42–82% (69%)[21,40,59]<br>*n* = 212 | 75–80% (78%)[28,32]<br>*n* = 323[a] | 49–96% (68%)[21,30,61]<br>*n* = 353 | 80%[28]<br>*n* = 222[a] | 5–100% (82%)[8,10,53–55,63]<br>*n* = 557 | Not reported |
| Dyspnoea | 18–88% (72%)[21,31,40,59]<br>*n* = 804 | 42–79% (62%)[22,23,28,31,32,39]<br>*n* = 1131 | 56–98% (94%)[21,29,30,44,61]<br>*n* = 619[b] | 89–91% (90%)[28,29]<br>*n* = 309[a,b] | 5–82% (52%)[8,10,53–55,63,67]<br>*n* = 726 | 18–46% (34%)[34,41,42,68]<br>*n* = 195 |
| Insomnia | 36–48% (45%)[31,40,59]<br>*n* = 726 | Not reported | 55–77% (65%)[29,30,61]<br>*n* = 359[b] | 51%[29]<br>*n* = 87[b] | 14–82% (47%)[8,10,50,53,54,63]<br>*n* = 419 | Not reported |
| Pain | 20–78% (41%)[21,31,39,40,59]<br>*n* = 878 | 14–63% (42%)[22,23,28,31]<br>*n* = 964 | 21–77% (68%)[21,29,30,44,61]<br>*n* = 1038[b] | 34–63% (49%)[28,29]<br>*n* = 309[a,b] | 21–64% (52%)[8,10,63,65]<br>*n* = 400 | 30–73% (49%)[33,34,41,42,48,68]<br>*n* = 292 |
| Mouth problems | 9[c]–45[d]% (27%)[40,59]<br>*n* = 146 | Not reported | 59–67% (63%)[29,61]<br>*n* = 150[b] | 48%[29]<br>*n* = 87[b] | 46[e]-58% (52%)[8,10]<br>*n* = 30 | Not reported |
| Cough | 24–44% (35%)[31,40,59]<br>*n* = 739 | Not reported | 59–80% (70%)[29,30,61]<br>*n* = 359[b] | 52%[29]<br>*n* = 87[b] | 46–47% (47%)[8,10]<br>*n* = 30 | Not reported |
| Anorexia | 11–43% (31%)[21,31,40,59]<br>*n* = 797 | Not reported | 11–81% (51%)[21,29,30,61]<br>*n* = 440[b] | 64%[29]<br>*n* = 87[b] | 21–64% (48%)[8,10,55,67]<br>*n* = 425 | Not reported |
| Depression | 6–59% (23%)[21,31,40,59,60]<br>*n* = 814 | Not reported | 17–77% (59%)[21,24,25,29,30,61]<br>*n* = 646[b,39] | 55%[29]<br>*n* = 87[b] | 8–51% (26%)[8,10,47,49–51,53,64,66]<br>*n* = 5985 | 25%[52]<br>*n* = 79 |
| Anxiety | 2–49% (30%)[21,31,40]<br>*n* = 737 | Not reported | 32–57% (53%)[21,30,61]<br>*n* = 353 | Not reported | 20–41% (27%)[8,10,51,53,66]<br>*n* = 161 | 25%[42]<br>*n* = 35 |
| Constipation | 12[f]–42% (37%)[31,40,59]<br>*n* = 667 | Not reported | 27–44% (36%)[29,61]<br>*n* = 150[b] | 25%[29]<br>*n* = 87[b] | 18–63% (28%)[8,10,62]<br>*n* = 502 | Not reported |
| Delirium/confusion | 29%[40]<br>*n* = 80 | 15–48% (17%)[22,28,39]<br>*n* = 481[a] | 13–33% (23%)[29,45]<br>*n* = 387[a,b] | 17–26% (22%)[28,29]<br>*n* = 309[a,b] | not reported | 13–68% (26%)[34,41,42,68]<br>*n* = 195 |
| Nausea | 2–48% (25%)[21,31,40,59]<br>*n* = 792 | 20%[32]<br>*n* = 60 | 4%[21]<br>*n* = 81 | Not reported | 30–44% (39%)[53–55]<br>*n* = 362 | 13–34% (13%)[34,42,68]<br>*n* = 159 |
| Edema | 33–44% (39%)[40,59]<br>*n* = 146 | 43%[39]<br>*n* = 90 | Not reported | Not reported | 42–73% (55%)[8,10,67]<br>*n* = 199 | 21%[42]<br>*n* = 35 |
| Dizziness | 21%[40]<br>*n* = 80 | 35%[32]<br>*n* = 60 | Not reported | Not reported | 37–50% (44%)[8,10,55]<br>*n* = 256 | Not reported |
| Pruritus | 12%[40]<br>*n* = 80 | Not reported | Not reported | Not reported | 49–73% (62%)[8,10,53–55]<br>*n* = 392 | 22%[42]<br>*n* = 35 |
| Weight loss | Not reported | Not reported | Not reported | Not reported | 18–32% (25%)[8,10]<br>*n* = 30 | Not reported |

Minimum–maximum prevalence, median (%), total number of patients in the included studies for each symptom (*n*) and references are shown.
CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure.
Terminal: last 2 weeks of life, last week, last 3 days, last 24 h or for CRF after discontinuation/declining of dialysis
[a] '*n*' can be under or overestimated because '*n*' is not exactly reported for each disease and each symptom.
[b] 5 patients with chronic lung disease other than COPD.
[c] Persistent thirst.
[d] Dry mouth or thirst.
[e] Dry mouth.
[f] Constipation or diarrhoea.

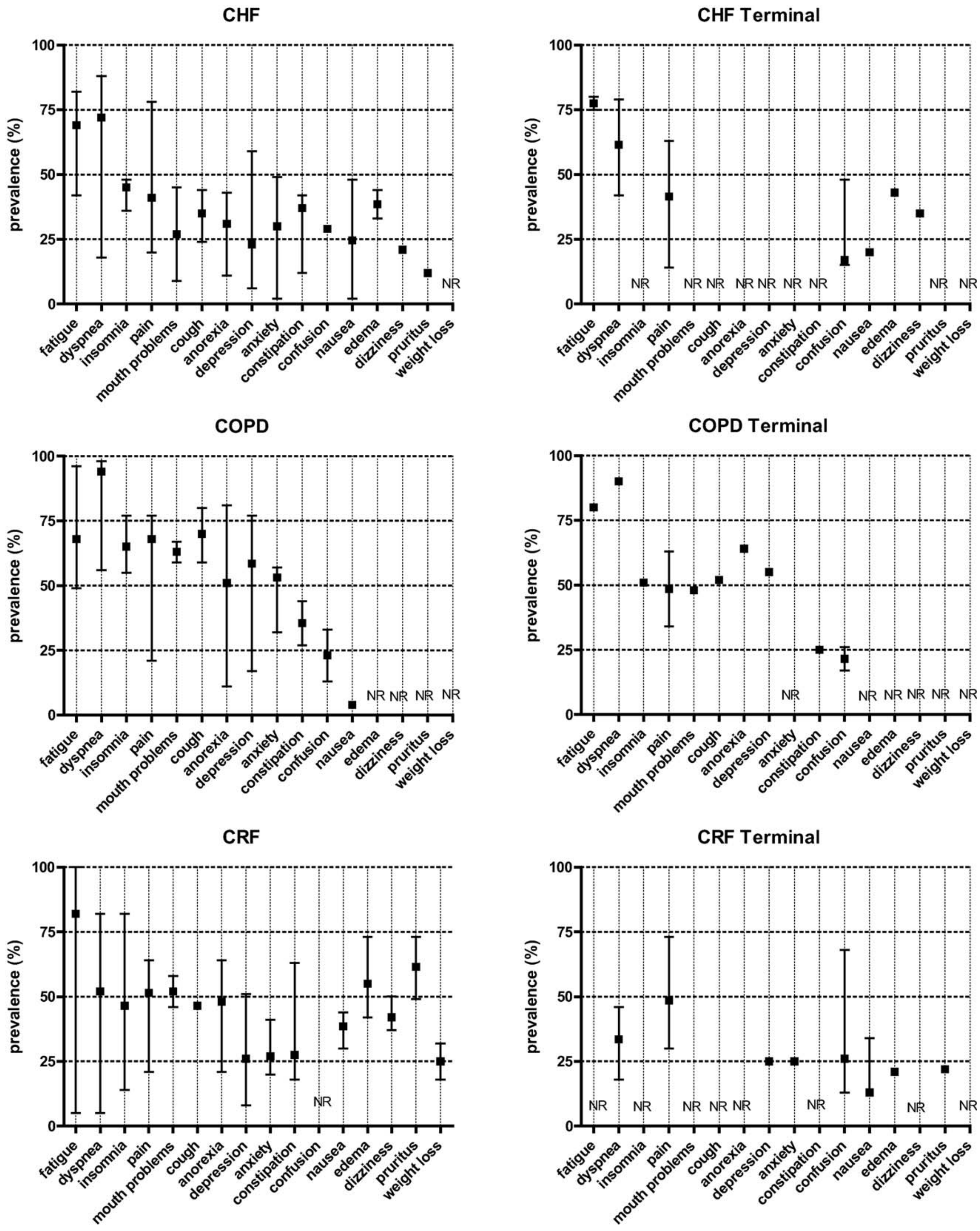

**Figure 3** Minimum, maximum and median prevalence of reported daily symptom burden in patients with end-stage congestive heart failure (CHF, left upper panel), terminal congestive heart failure (CHF terminal, right upper panel), end-stage chronic obstructive pulmonary disease (COPD, left middle panel), terminal chronic obstructive pulmonary disease (COPD terminal, right middle panel), Chronic renal failure (CRF, left lower panel) or terminal chronic renal failure (CRF terminal, right lower panel). NR, not reported.

depression are reported as less severe and occurring less frequently the later the interview is conducted.[38]

Other studies relied on charts or medical records for identifying symptoms.[39–42] These sources provide only indirect reporting of the daily symptom burden, potentially under representing symptoms that are not recognised by caregivers such as nurses and physicians. Moreover, these sources can also include interpretations. For example, in two of the studies, the presence of depression was based upon the use of anti-depressive medication. However, this will underestimate the prevalence of depression.[24]

Second, in the currently available literature, there is no clear and commonly accepted definition of end-of-life or end-stage.[43] We included studies that were found by searching for the keywords 'palliative care', 'hospice care', 'terminal care', 'terminally ill' or 'end-of-life'. However, these labels signify varying degrees of prognosis. This could probably influence the reported daily symptom burden. For instance, in the study of Edmonds, *et al.*, symptom burden of patients with COPD has been studied retrospectively in the last year and the last week of life. For all the studied symptoms, a lower prevalence has been reported in the last week compared with the last year of life.[29] In patients with CRF who withdrew from dialysis, Chater, *et al.*[42] have shown that in the last 24 h of life symptom prevalence decreased. On the contrary, in the Study to Understand Prognoses and Preferences for Outcome and Risk of Treatments (SUPPORT), it was found that the number of patients with CHF who reported symptoms such as severe pain or dyspnoea increased as death came nearer.[22] This could probably be partly explained by the fact that symptom burden in the last 3 days of life has only been studied by proxy reporting and in the last 6 months symptom burden has been studied by patient and proxy reporting. Although the exact relationship is not known, it is highly plausible that symptom burden is related to prognoses.

Third, patient selection criteria varied between the studies, introducing variability in patient characteristics. Some studies included only patients who were hospitalised during an acute exacerbation,[22,44,45] other studies selected only outpatients.[25] Patients included in prospective studies, those recognised as being at the end of life, could conceivably have other characteristics than patients included in retrospective studies, patients who have died.[46] In some studies, considerably co-existing morbidities were present,[8,34,45,47–50] whereas in others co-morbidity was not reported.

Fourth, definition and measurement of symptoms varied across the studies. Depression for example was defined as neurotic depression (DSM-IIIR),[51] major depression (DSM-IV),[52] feelings of depression,[21] low mood,[30] feeling sad,[8] a score of ≥8 points on the depression scale of Hospital Anxiety and Depression Scale (HADS),[53] a score of ≥16 points on the Center for Epidemiologic Study-Depression survey (CES-D),[25] a score of ≥11 points on the Geriatric Depression Scale (GDS)[24] or Beck Depression Inventory (BDI).[47] The criteria for determining when a symptom was present and to what degree also varied. A symptom was considered as present in the various studies, if it was experienced all the time or sometimes,[30] if it was mild to very severe,[54] if it was moderately severe or extremely severe at least half of the time,[22] a little bit, moderately, much or very much present[55] or the symptom was uncontrolled.[23] The length of the recall period varied from 24 h to 1 year.

## Conclusions and implications

The need for palliative care for patients with end-stage chronic organ failure has been previously asserted.[7,8,10,56] The degree daily symptom burden of patients with end-stage CHF, COPD or CRF that we found in this systematic review adds to such an assertion. Unfortunately, the heterogeneity and limitations of the study designs we reviewed do not permit a comparison of symptom prevalence between patients with end-stage CHF, COPD or CRF.

This limitation highlights the methodological challenges of research in end-of-life care as have been previously described.[46,57,58] The resulting limited understanding of daily symptom burden in patients with CHF, COPD or CRF at the end of their life hampers efforts to develop patient-centred intensive management program aimed at reducing suffering and/or improving quality of life of patients with end-stage chronic organ failure and their families by preventing, relieving or soothing self-perceived daily symptoms. Further prospective and longitudinal research in which the views of patients, their families and their treating physician are taken into account is needed. Only then it may be possible to optimise palliative care and symptom management in patients with CHF, COPD or CRF at the end of their life.

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## References

1 From the Centers for Disease Control and Prevention. Public health and aging: trends in aging – United States and worldwide. *JAMA* 2003; **289**: 1371–1373.

2 Bleumink, GS, Knetsch, AM, Sturkenboom, MC, Straus, SM, Hofman, A, Deckers, JW, *et al*. Quantifying the heart failure epidemic: prevalence, incidence rate, lifetime risk and prognosis of heart failure The Rotterdam Study. *Eur Heart J* 2004; **25**: 1614–1619.

3 Feenstra, TL, van Genugten, ML, Hoogenveen, RT, Wouters, EF, Rutten-van Molken, MP. The impact of aging and smoking on the future burden of chronic obstructive pulmonary disease: a model analysis in the Netherlands. *Am J Respir Crit Care Med* 2001; **164**: 590–596.

4 Stengel, B, Billon, S, Van Dijk, PC, Jager, KJ, Dekker, FW, Simpson, K, *et al*. Trends in the incidence of renal replacement therapy for end-stage renal disease in Europe, 1990–1999. *Nephrol Dial Transplant* 2003; **18**: 1824–1833.

5 Hauptman, PJ, Havranek, EP. Integrating palliative care into heart failure care. *Arch Intern Med* 2005; **165**: 374–378.

6 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**: 1000–1006.

7 Curtis, JR. Palliative and End-of-life Care for Patients with Severe COPD. *Eur Respir J* 2007.

8 Weisbord, SD, Carmody, SS, Bruns, FJ, Rotondi, AJ, Cohen, LM, Zeidel, ML, *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**: 1345–1352.

9 Tranmer, JE, Heyland, D, Dudgeon, D, Groll, D, Squires-Graham, M, Coulson, K. 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**: 420–429.

10 Saini, T, Murtagh, FE, Dupont, PJ, McKinnon, PM, Hatfield, P, Saunders, Y. Comparative pilot study of symptoms and quality of life in cancer patients and patients with end stage renal disease. *Palliat Med* 2006; **20**: 631–636.

11 Riedinger, MS, Dracup, KA, Brecht, ML. Quality of life in women with heart failure, normative groups, and patients with other chronic conditions. *Am J Crit Care* 2002; **11**: 211–219.

12 Grande, GE, Farquhar, MC, Barclay, SI, Todd, CJ. The influence of patient and carer age in access to palliative care services. *Age Ageing* 2006; **35**: 267–273.

13 Mast, KR, Salama, M, Silverman, GK, Arnold, RM. End-of-life content in treatment guidelines for life-limiting diseases. *J Palliat Med* 2004; **7**: 754–773.

14 Rabe, KF, Hurd, S, Anzueto, A, Barnes, PJ, Buist, SA, Calverley, P, *et al*. Global strategy for the diagnosis, management, and prevention of COPD - 2006 update. *Am J Respir Crit Care Med* 2007; **176**: 532–555.

15 Murray, SA, Boyd, K, Kendall, M, Worth, A, Benton, TF, Clausen, H. Dying of lung cancer or cardiac failure: prospective qualitative interview study of patients and their carers in the community. *BMJ* 2002; **325**(7370): 929–934.

16 Fox, E, Landrum-McNiff, K, Zhong, Z, Dawson, NV, Wu, AW, Lynn, J. Evaluation of prognostic criteria for determining hospice eligibility in patients with advanced lung, heart, or liver disease. SUPPORT Investigators. Study to understand prognoses and preferences for outcomes and risks of treatments. *JAMA* 1999; **282**: 1638–1645.

17 Murray, SA, Kendall, M, Boyd, K, Sheikh, A. Illness trajectories and palliative care. *BMJ* 2005; **330**(7498): 1007–1011.

18 Miravitlles, M, Calle, M, Alvarez-Gutierrez, F, Gobartt, E, Lopez, F, Martin, A. Exacerbations, hospital admissions and impaired health status in chronic obstructive pulmonary disease. *Qual Life Res* 2006; **15**: 471–480.

19 Murtagh, FE, Preston, M, Higginson, I. Patterns of dying: palliative care for non-malignant disease. *Clin Med* 2004; **4**: 39–44.

20 Janssen, DJ, Wouters, EF, Schols, JM, Spruit, MA. Self-perceived symptoms and care needs of patients with severe to very severe chronic obstructive pulmonary disease, congestive heart failure or chronic renal failure and its consequences for their closest relatives: the research protocol. *BMC Palliat Care* 2008; **7**: 5.

21 Walke, LM, Gallo, WT, Tinetti, ME, Fried, TR. The burden of symptoms among community-dwelling older persons with advanced chronic disease. *Arch Intern Med* 2004; **164**: 2321–2324.

22 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. 5): S101–S109.

23 Formiga, F, Olmedo, C, Lopez-Soto, A, Navarro, M, Culla, A, Pujol, R. Dying in hospital of terminal heart failure or severe dementia: the circumstances associated with death and the opinions of caregivers. *Palliat Med* 2007; **21**: 35–40.

24 Lacasse, Y, Rousseau, L, Maltais, F. Prevalence of depressive symptoms and depression in patients with severe oxygen-dependent chronic obstructive pulmonary disease. *J Cardiopulm Rehabil* 2001; **21**: 80–86.

25 Stapleton, RD, Nielsen, EL, Engelberg, RA, Patrick, DL, Curtis, JR. Association of depression and life-sustaining treatment preferences in patients with COPD. *Chest* 2005; **127**: 328–334.

26 Solano, JP, Gomes, B, Higginson, IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. *J Pain Symptom Manage* 2006; **31**: 58–69.

27 Murtagh, FE, Addington-Hall, J, Higginson, IJ. The prevalence of symptoms in end-stage renal disease: a systematic review. *Adv Chronic Kidney Dis* 2007; **14**: 82–99.

28 Lynn, J, Teno, JM, Phillips, RS, Wu, AW, Desbiens, N, Harrold, J, *et al*. Perceptions by family members of the dying experience of older and seriously ill patients. SUPPORT Investigators. Study to understand prognoses and preferences for outcomes and risks of treatments. *Ann Intern Med* 1997; **126**: 97–106.

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

30 Elkington, H, White, P, Addington-Hall, J, Higgs, R, Edmonds, P. The healthcare needs of chronic obstructive pulmonary disease patients in the last year of life. *Palliat Med* 2005; **19**: 485–491.

31 McCarthy, M, Lay, M, Addington-Hall, J. Dying from heart disease. *J R Coll Physicians Lond* 1996; **30**: 325–328.

32 Sullivan, MD, OMeara, ES. Heart failure at the end of life: symptoms, function, and medical care in the Cardiovascular Health Study. *Am J Geriatr Cardiol* 2006; **15**: 217–225.

33 Cohen, LM, Germain, MJ, Woods, AL, Mirot, A, Burleson, JA. The family perspective of ESRD deaths. *Am J Kidney Dis* 2005; **45**: 154–161.

34 Cohen, LM, Germain, M, Poppel, DM, Woods, A, Kjellstrand, CM. Dialysis discontinuation and palliative care. *Am J Kidney Dis* 2000; **36**: 140–144.

35 Klinkenberg, M, Smit, JH, Deeg, DJ, Willems, DL, Onwuteaka-Philipsen, BD, van der Wal, G. Proxy reporting in after-death interviews: the use of proxy respondents in retrospective assessment of chronic diseases and symptom burden in the terminal phase of life. *Palliat Med* 2003; **17**: 191–201.

36 Higginson, I, Priest, P, McCarthy, M. Are bereaved family members a valid proxy for a patient's assessment of dying? *Soc Sci Med* 1994; **38**: 553–557.

37 Higginson, I, Wade, A, McCarthy, M. Palliative care: views of patients and their families. *BMJ* 1990; **301** (6746): 277–281.

38 McPherson, CJ, Addington-Hall, JM. How do proxies' perceptions of patients' pain, anxiety, and depression change during the bereavement period? *J Palliat Care* 2004; **20**: 12–19.

39 Zambroski, CH, Moser, DK, Roser, LP, Heo, S, Chung, ML. Patients with heart failure who die in hospice. *Am Heart J* 2005; **149**: 558–564.

40 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**: 213–217.

41 Brunier, G, Naimark, DM, Hladunewich, MA. Meeting the guidelines for end-of-life care. *Adv Perit Dial* 2006; **22**: 175–179.

42 Chater, S, Davison, SN, Germain, MJ, Cohen, LM. Withdrawal from dialysis: a palliative care perspective. *Clin Nephrol* 2006; **66**: 364–372.

43 Lorenz, KA, Lynn, J, Dy, SM, Shugarman, LR, Wilkinson, A, Mularski, RA, *et al*. Evidence for improving palliative care at the end of life: a systematic review. *Ann Intern Med* 2008; **148**: 147–159.

44 Claessens, MT, Lynn, J, Zhong, Z, Desbiens, NA, Phillips, RS, Wu, AW, *et al*. Dying with lung cancer or chronic obstructive pulmonary disease: insights from SUPPORT. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *J Am Geriatr Soc* 2000; **48**(Suppl. 5): S146–S153.

45 Lynn, J, Ely, EW, Zhong, Z, McNiff, KL, Dawson, NV, Connors, A, *et al*. Living and dying with chronic obstructive pulmonary disease. *J Am Geriatr Soc* 2000; **48**(Suppl. 5): S91–S100.

46 Bach, PB, Schrag, D, Begg, CB. Resurrecting treatment histories of dead patients: a study design that should be laid to rest. *JAMA* 2004; **292**: 2765–2770.

47 Wuerth, D, Finkelstein, SH, Finkelstein, FO. The identification and treatment of depression in patients maintained on dialysis. *Semin Dial* 2005; **18**: 142–146.

48 Cohen, LM, McCue, JD, Germain, M, Kjellstrand, CM. Dialysis discontinuation. A 'good' death? *Arch Intern Med* 1995; **155**: 42–47.

49 Lopes, AA, Bragg, J, Young, E, Goodkin, D, Mapes, D, Combe, C, *et al*. Depression as a predictor of mortality and hospitalization among hemodialysis patients in the United States and Europe. *Kidney Int* 2002; **62**: 199–207.

50 Iliescu, EA, Coo, H, McMurray, MH, Meers, CL, Quinn, MM, Singer, MA, *et al*. Quality of sleep and health-related quality of life in haemodialysis patients. *Nephrol Dial Transplant* 2003; **18**: 126–132.

51 Aghanwa, HS, Morakinyo, O. Psychiatric complications of hemodialysis at a kidney center in Nigeria. *J Psychosom Res* 1997; **42**: 445–451.

52 Cohen, LM, Dobscha, SK, Hails, KC, Pekow, PS, Chochinov, HM. Depression and suicidal ideation in patients who discontinue the life-support treatment of dialysis. *Psychosom Med* 2002; **64**: 889–896.

53 McCann, K, Boore, JR. Fatigue in persons with renal failure who require maintenance haemodialysis. *J Adv Nurs* 2000; **32**: 1132–1142.

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

55 Merkus, MP, Jager, KJ, Dekker, FW, de Haan, RJ, Boeschoten, EW, Krediet, RT. 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**: 1163–1170.

56 Pantilat, SZ, Steimle, AE. Palliative care for patients with heart failure. *JAMA* 2004; **291**: 2476–2482.

57 Teno, JM. Measuring end-of-life care outcomes retrospectively. *J Palliat Med* 2005; **8**(Suppl. 1): S42–S49.

58 Fowler, FJ, Jr, Coppola, KM, Teno, JM. Methodological challenges for measuring quality of care at the end of life. *J Pain Symptom Manage* 1999; **17**: 114–119.

59 Anderson, H, Ward, C, Eardley, A, Gomm, SA, Connolly, M, Coppinger, T, *et al*. The concerns of patients under palliative care and a heart failure clinic are not being met. *Palliat Med* 2001; **15**: 279–286.

60 Vig, EK, Pearlman, RA. Quality of life while dying: a qualitative study of terminally ill older men. *J Am Geriatr Soc* 2003; **51**: 1595–1601.

61 Skilbeck, J, Mott, L, Page, H, Smith, D, Hjelmeland-Ahmedzai, S, Clark, D. Palliative care in chronic obstructive airways disease: a needs assessment. *Palliat Med* 1998; **12**: 245–254.

62 Yasuda, G, Shibata, K, Takizawa, T, Ikeda, Y, Tokita, Y, Umemura, S, *et al*. Prevalence of constipation in continuous ambulatory peritoneal dialysis patients and comparison with hemodialysis patients. *Am J Kidney Dis* 2002; **39**: 1292–1299.

63 Kimmel, PL, Emont, SL, Newmann, JM, Danko, H, Moss, AH. ESRD patient quality of life: symptoms, spiritual beliefs, psychosocial factors, and ethnicity. *Am J Kidney Dis* 2003; **42**: 713–721.

64 Craven, JL, Rodin, GM, Johnson, L, Kennedy, SH. The diagnosis of major depression in renal dialysis patients. *Psychosom Med* 1987; **49**: 482–492.

65 Davison, SN. Pain in hemodialysis patients: prevalence, cause, severity, and management. *Am J Kidney Dis* 2003; **42**: 1239–1247.

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

67 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**: 229–233.

68 Noble, H, Rees, K. Caring for people who are dying on renal wards: a retrospective study. *EDTNA ERCA J* 2006; **32**: 89–92.