Age and Ageing 2005; **34:** 218–227
doi:10.1093/ageing/afi054

SYSTEMATIC REVIEWS

Prediction of appropriate timing of palliative care for older adults with non-malignant life-threatening disease: a systematic review

PETER A. COVENTRY[1], GUNN E. GRANDE[1], DAVID A. RICHARDS[2], CHRIS J. TODD[1]

[1]School of Nursing, Midwifery and Social Work, The University of Manchester, Oxford Road, Manchester M13 9PL, UK
[2]Department of Health Sciences, Seebohm Rowntree Building, University of York, University Road, York YO10 5DD, UK

Address correspondence to: C. J. Todd. Fax: (+44) 0161 275 5335. Email: chris.todd@manchester.ac.uk

Abstract

Background: most people in contemporary western society die of the chronic diseases of old age. Whilst palliative care is appropriate for elderly patients with chronic, non-malignant disease, few of these patients access such care compared with cancer patients. Objective referral criteria based on accurate estimation of survival may facilitate more timely referral of non-cancer patients most appropriate for specialist palliative care.
Objective: to identify tools and predictor variables that might aid clinicians estimate survival and assess palliative status in non-cancer patients aged 65 years and older.
Methods: systematic review and quality assessment using criteria modified from the literature.
Results: 11 studies that evaluated prognoses in hospitalised and community-based older adults with non-malignant disease were identified. Key generic predictors of survival were increased dependency of activities of daily living, presence of comorbidities, poor nutritional status and weight loss, and abnormal vital signs and laboratory values. Disease-specific predictors of survival were identified for dementia, chronic obstructive pulmonary disorder and congestive heart failure. No study evaluated the relationship between survival and palliative status.
Conclusion: prognostic models that attempt to estimate survival of ≤6 months in non-cancer patients have generally poor discrimination, reflecting the unpredictable nature of most non-malignant disease. However, a number of generic and disease-specific predictor variables were identified that may help clinicians identify older, non-cancer patients with poor prognoses and palliative care needs. Simple, well-validated prognostic models that provide clinicians with objective measures of palliative status in non-cancer patients are needed. Additionally, research that evaluates the effect of general and specialist palliative care on psychosocial outcomes in non-cancer patients and their carers is needed.

Keywords: *palliative care, prognosis, non-cancer, chronic disease, elderly*

Introduction

In developed countries with ageing populations more people now die of chronic circulatory and respiratory conditions than of cancer [**1**, 2]. At least half of all cancer patients in the UK receive some kind of specialist palliative care during the course of their illness [**3**]. This type of care is normally delivered by specialist multi-disciplinary teams whose activities are focused on a significant minority of people with advanced incurable disease, typically cancer patients [3]. By contrast, general palliative care has been defined as a vital and routine part of clinical practice that aims to promote physical and psychosocial health, regardless of diagnosis or prognosis [3, 4]. Whilst it is widely acknowledged that palliative care is appropriate for patients with life-threatening, non-malignant disease, there is strong evidence of unmet need for symptom control, psychosocial and family support, informed and open communication and choice at end-of-life among this population [**5–7**]. Furthermore, there is limited evidence that at least a fifth of patients with end-stage, non-malignant disease have comparable levels of symptom severity and psychosocial needs as cancer patients in receipt of specialist palliative care [**8**]. In the UK, 95% of patients receiving inpatient hospice care, home care or day hospice care have a diagnosis of cancer [9].

It does not logically follow that because there is evidence of inequities of access to hospice care and unmet needs among non-cancer patients that specialist palliative care

services should be extended to this group. There are many barriers to extending specialist palliative care services to older patients dying from non-malignant disease. These include concerns that such an expansion might lead to skills and funding shortages and, in turn, compromise the ability of existing specialist palliative care teams to provide care to cancer patients. In addition, little is known about the acceptability of specialist palliative care services among non-cancer patients—the attitudes of this group of potential new users has been peculiarly overlooked in efforts to extend the reach of specialist palliative care. But perhaps the main barrier to extending specialist palliative care services to older, non-cancer patients relates to clinicians' reluctance and/or inability to define palliative status and predict time to death in this group [**8**].

In the UK, disagreements between medical professionals about the suitability of patients for palliative care are commonplace [10, **11**]. Clinical predictions of survival for terminally ill cancer patients are generally over-optimistic, in some cases up to a factor of about five [**12**]. Compared with cancer, determining prognosis is more complicated in life-threatening, non-malignant disease. Most of these diseases have 'entry–re-entery' death trajectories, involving episodic, acute exacerbations, frequent hospitalisation, stabilisation and steady decline, making determination of palliative status and referral to hospice care more problematic [**13**].

The development of objective referral criteria, based on reliable prognostic estimates, may overcome some of the problems related to the identification of older patients dying of non-malignant disease who may benefit from specialist palliative care. A number of prognostic tools have been developed to assist clinicians in assessing short-term survival in terminally ill cancer patients [**14, 15**], but their usefulness in non-cancer patients is not known. We have therefore undertaken a systematic review to identify and evaluate potential decision-making tools and predictor variables that might aid clinicians determine short-term (≤6 months) survival in older, non-cancer patients. A survival estimate of ≤6 months is used to decide eligibility for Medicaid/Medicare hospice benefits [16] and Disability Living Allowance under special rules [17] and could therefore provide some guidance about appropriateness and timing of specialist palliative care for older, non-cancer patients.

Methods

Search strategy

Relevant articles were identified and retrieved from electronic searches of Medline, EMBASE, PsychINFO, CINAHL, British Nursing Index, HMIC, ERIC, ASSIA, Social Sciences Citation Index, Science Citation Index, Regard and Zetoc. The Cochrane Library was searched using an adapted version of the search strategy. All electronic searches were undertaken in November 2003 and date from the first issue of the respective databases. Unpublished sources and work in progress were searched using SIGLE, Current Controlled Trials (metaRegister of Controlled Trials), National Research Register and Research Findings Electronic Register. All searches were supplemented by database auto-alert services (up to March 2004), searches of web resources in palliative and supportive care, reviews of reference lists of identified studies, consultation with experts in the field and correspondence with authors.

The search strategy was devised in accordance with the guidelines and recommendations of the Cochrane Collaboration [**18**] and Centre for Reviews and Dissemination [**19**]. The search was not restricted by language of publication nor by study design and/or quality. Keywords (single MeSH and text words) were combined to identify all articles that evaluated the use of prognostic tools, variables or risk factors to aid estimation of survival or determine palliative status in adults aged ≥65 years with non-malignant life-threatening disease. The full search strategy is available from the corresponding author (C.J.T.). An article was excluded if: (i) the study population was <65 years, consisted exclusively of cancer, trauma or non-terminal patients; (ii) it described patient- or family-based decision aids; (iii) the study aimed to identify patients appropriate for therapeutic rather than palliative interventions; (iv) it was a review or an editorial.

Please see Appendix 1 and 2 in the supplementary data on the journal website (www.ageing.oupjournals.org) for a review of the data abstraction and quality assessment process.

Due to the heterogeneity of studies a formal meta-analysis of results was not appropriate. A non-statistical descriptive approach was used to contrast and compare the main characteristics and findings of each study.

Results

Electronic and hand searches identified 979 citations. Initial screening of the electronic search resulted in selection of 85 non-duplicate abstracts for further analysis (Figure 1). Of these, 48 merited full-text analysis and were read by a member of the review team (P.A.C.). Thirty articles did not meet the inclusion criteria. Of the 18 remaining studies, inclusion was uncertain in 12, which were independently assessed by two other members of the review team (C.J.T./G.E.G.). Following a consensus meeting, 11 studies were included in the review. Please see Appendix 3 and 4 in the supplementary data on the journal website for the results of the quality assessment exercise.

The study characteristics and main findings of the 11 studies are presented in Table 1. Three studies reported disease-specific prognostic models [**27–29**], two reported generic prognostic models [**30, 31**], three evaluated predictor variables for short-term (≤6 months) survival in dementia patients [**32–34**] and three evaluated predictor variables for longer-term survival (≤5 years) in chronic obstructive pulmonary disorder (COPD) [**35–37**].

Disease-specific prognostic models

Of the three (grade A) studies that reported disease-specific prognostic models, two (Knaus [**27**], Fox [**28**]) evaluated the accuracy of methods to estimate 6-month survival in a subset of patients in the SUPPORT trial with a diagnosis of COPD, congestive heart failure (CHF) and end-stage liver disease (ESLD). Although the SUPPORT model, combined

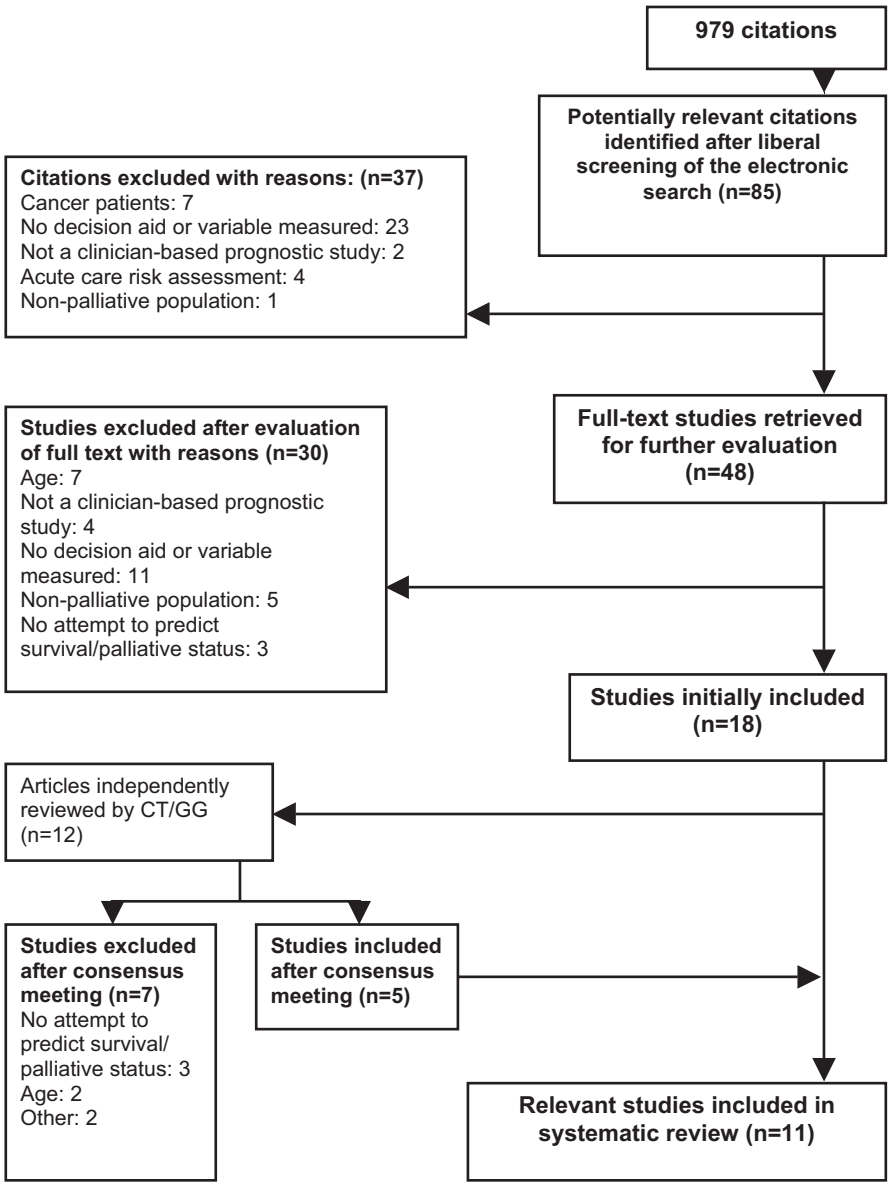

Figure 1. Flow chart of study selection.

with physicians' own estimate, had good predictive power when applied to all disease groups (ROC curve area = 0.82), it had poor positive discrimination when applied to the group that incorporated COPD, CHF and ESLD patients (n = 1111 (ROC curve area = 0.75)).

The (US) National Hospice Palliative Care Organization (NHPCO) guidelines for determining prognosis in non-cancer diseases [**38**] were similarly ineffective in predicting ≤6 month survival in a group of SUPPORT patients with COPD, CHF and ESLD: 81% of COPD patients with evidence of cor pulmonale and 77% with hypoxaemia (≤55 mm Hg while on supplemental oxygen) were alive at 6 months; 73% of CHF patients with ejection faction ≤20% and 75% with documented arrhythmia were alive at 6 months; 69% of ESLD patients with documented cachexia and 45% with creatinine ≥153 μmol/l were alive at 6 months [**28**]. On the basis of these results neither the SUPPORT model nor prognostic criteria analogous to the NHPCO guidelines are able to predict accurately 6-month survival in seriously ill patients hospitalised with COPD, CHF or ESLD.

By contrast, Lee *et al.* showed that a prognostic model, based on routine clinical and demographic data available on admission, may be used to predict 30-day and 1-year survival in some elderly community-based CHF patients, but the model has yet to be validated in a UK setting [**29**]. A corresponding risk index may aid clinicians in counselling patients and families about end-of-life treatment and care.

Generic prognostic models

Only one (grade B) study measured the ability of a dedicated prognostic tool—the Palliative Prognostic (PaP) score—to improve end-of-life clinical decision making in patients with non-malignant disease [**30**]. The PaP score comprises four

Table 1. Study characteristics and main findings

1st author and ref	Population and setting	Design and follow-up	Prognostic variables/model	Outcome(s)	Main findings
Knaus [**27**] Grade A	4301 (median age 65 years; 57% male) and 4804 (median age 65 years; 56% male) seriously ill patients admitted to one of five tertiary academic medical centres, USA.	Prospective cohort study to develop (phase I) and validate (phase II) a prognostic model that estimates survival in seriously ill adults hospitalised with 1 of 9 illnesses. Patients followed up for 180 days after study entry.	Diagnosis (acute respiratory failure, COPD, CHF, ESLD, coma, colon cancer, lung cancer, MSOF with cancer, MSOF with sepsis); age; number of days in hospital before study entry; presence of cancer; neurological function (modified Glasgow coma scale); 11 physiological variables (albumin [g/dl]; bilirubin [mg/dl]; heart rate [beats/min]; leukocyte count [thousands]; mean blood pressure [mm Hg]; PaO_2/FiO_2; respiratory rate [breaths/min] serum creatinine [mg/dl]; serum sodium [mEq/l]; temperature [°C])	180-day mortality rates and prognostic accuracy of SUPPOT model compared with existing prognostic system (APACHE III) and physician's own estimates.	In phase I, 2072 patients (48%) died within 6 months of study entry. The ROC curve area for prediction of 180-day survival was 0.79 in phase 1 and 0.78 in phase II. The best survival estimate (for total study population) combined the SUPPORT model and the physician's own estimates (ROC curve area = 0.82), and enabled identification of patients at both extremes of risk.
Fox [**28**] Grade B	2607 seriously ill adults hospitalised with COPD, CHF or ESLD, and who survived to discharge from one of five tertiary care academic centres in USA.	Retrospective validation study using prospectively collected data from phase 1 and phase 2 of SUPPORT with a 6-month follow-up.	Readmission within 2 months, home care after discharge, ADL dependency ≥3 (modified Katz Index of ADL Scale), weight loss ≥12.3 kg within 2 months, albumin <25 g/l. Disease-specific variables: cor pulmonale, $PO_2 \leq 55$ mm Hg while receiving oxygen; ejection fraction ≤20%, arrhythmia; cachexia, creatinine ≥153 μmol/l.	Presence/absence of five general and two disease-specific clinical variables, SUPPORT multivariate model, hospice discharge and three combinations of hospice eligibility (broad, intermediate and narrow inclusion) based on NHPCO guidelines.	75% of the total sample survived >6 months after discharge. Broad inclusion criteria (one of seven variables) identified 923 patients eligible for hospice care (70% survived >6 months); intermediate inclusion criteria (three ofseven variables) identified 300 patients (65% survived >6 months); narrow inclusion criteria (five of seven variables) identified 19 patients (53% survived >6 months). Sensitivity was low (<50%) for all inclusion criteria.
Lee [**29**] Grade A	2624 (mean age 76.3 [SD = 11.2]; 50.5% female) and 1407 (mean age 75.3 [SD = 11.8] years; 50.5% female) patients with heart failure admitted to multiple hospitals in Ontario, Canada.	Retrospective cohort study to derive and validate predictive model of mortality in hospitalised heart failure patients followed-up for 1 year.	Age, vital signs (blood pressure [mm Hg]; heart rate [beats/min]; oxygen saturation [%]; respiratory rate [breaths/min]); laboratory values (haemoglobin [g/dl]; leukocyte count [/mm_2]; serum creatinine [mg/dl]; serum sodium [mEq/l]; urea nitrogen [mg/dl]; glucose [mg/dl]) and comorbidities (Charlson comorbidity index).	All-cause 30-day and 1-year mortality.	Multivariate predictors of both 30-day and 1-year mortality were older age, lower systolic blood pressure, higher respiratory rate, higher urea nitrogen level (all $P < 0.001$) and lower sodium concentration ($P < 0.01$). Low haemoglobin concentration was predictive of 1-year death ($P = 0.02$). Comorbidities associated with mortality in both models were cerebrovascular disease, dementia, COPD, cirrhosis and cancer. A risk index (stratified by quintile of risk) was constructed for both 30-day and 1-year mortality and identified individuals at low-risk and high-risk of death. In the derivation cohort the ROC curve area for the 30-day model was 0.80 and 0.77 for the 1-year model.

continued

Table 1. *continued*

Glare [**30**] Grade B	65 (median age 67 [range 27–92] years; 42 males) patients with non-malignant disease referred for a palliative medicine consultation at a university hospital, an affiliated community hospital and local nursing homes in Sydney, Australia.	Prospective cohort study of patients with diagnoses other than cancer referred to one of the authors for palliative medicine consultation between Jan 2000 and April 2002. Patients followed-up for 1 year.	PaP score comprising four clinical and two laboratory parameters: presence/absence of dyspnoea; presence/absence of anorexia; CPS; KPS; white blood cell count; lymphocyte count. Each item is allocated a partial score. The sum total (0–17.5) is used to classify patients into high (>70%), intermediate (30–70%) and low (<30%) risk groups for surviving 30 days.	Prognostic accuracy of PaP score in determining probability of surviving ≥1 month in non-cancer patients.	PaP score able to divide heterogeneous population with various non-malignant diseases into 3 iso-prognostic groups (A-C) independent of diagnosis. In group A, 14 out of 16 (86%) patients with >70% probability of surviving 30 days were alive at 1 month (95% CI, 88- . . .); in group B, 9 out of 16 patients (56%) with 30–70% probability of surviving 30 days were alive at 1 month (95% CI, 9–48); in group C, 3 out of 33 (3%) patients with <30% probability of surviving 30 days were alive at 1 month (95% CI, 3–6).
Walter [**31**] Grade A	1495 (mean age 81 [SD = 8] years; 67% female) patients discharged from a tertiary academic hospital and 1427 (mean age 79 [SD = 7] years; 61% female) patients discharged from a community teaching hospital, USA.	Retrospective analyses of two randomised trials to develop and validate a prognostic index for 1-year mortality of older hospitalised adults. Patients followed-up for 1 year.	Age, gender, ethnicity, marital status, independence in five ADLs (modified Katz Index of ADLs), comorbidities (Charlson comorbidity index), length-of-stay, discharge destination, main reason for admission, laboratory values (albumin [g/dl]; serum creatinine [mg/dl])	Prediction of 1-year post-hospital mortality in hospitalised older (aged ≥70 years) adults using demographic and clinical risk factors.	In the derivation cohort multivariate analyses identified 6 independent risk factors associated with mortality which were then weighted using an additive point scoring system: male sex (1 point); number of dependent ADLs (1–4 ADLs = 2 points; 5ADLs = 5 points); CHF (2 points); cancer (solitary = 3 points; metastatic = 8 points); creatinine >3.0 mg/dl (2 points); low albumin levels (3.0–3.4 g/dl = 1 point; <3.0 g/dl = 2 points). The ROC curve area for the point scoring system was 0.75 in the derivation cohort and 0.79 in the validation cohort.
Hanrahan [**32**] Grade C	11 (mean age 88 [range 81–102] years; 64% female) patients with end-stage dementia home-based hospice patients, Chicago, USA.	Prospective cohort pilot study of enrolment criteria for admission to hospice care for end-stage dementia patients. Patients followed-up until death or until end of the two-year study.	Presence of severe dementia (GDS stage 7); mental status (MSQ); medical complications, ADLs (no instrument reported), caregiver interest in hospice care; service characteristics.	Survival time in days between hospice enrolment and patient death or, for survivors, the end of the study.	Median survival time was 5 months (mean 7 months). The deceased patients ($n = 8$) had a mean survival time of 3 months (range 2–365 days). The enrolment criteria successfully identified patients appropriate for hospice care according to standard admission criteria in the USA.
Luchins [**33**] Grade B	42 (mean age 84 [SD = 9.2] years; 70% female) severely demented patients with a recent or current history of related medical complications enrolled in 9 Midwestern home-based and institutional hospice programmes, USA.	Two-year prospective cohort study of previously developed hospice enrolment criteria and a retrospective assessment of the utility of NHPCO guidelines to appropriately identify dementia patients eligible for hospice care. All patients followed-up for 6 months.	Cognitive impairment (MSQ), ADLs (OARS), Medical Complications Checklist (physician survey), survival time, performance ratings (appetite, nourishment, mobility), FAST scale, palliative care plan.	Survival time (number of days between hospice enrolment and death or study end).	Hospice enrolment criteria identified a group of patients with a median survival time of 4 months (mean 6.9 [SD = 7.3]). In the univariate model strong predictors of survival were FAST scores ($P < 0.01$) performance ratings (mobility [$P < 0.001$]; appetite [$P < 0.01$]) and total score on ADLs ($P < 0.01$). Using NHPCO guidelines a subgroup of patients (FAST score stage 7C) with high mortality and short survival time may be identified for appropriate hospice care.

Table 1. *continued*

1st author and ref	Population and setting	Design and follow-up	Prognostic variables/model	Outcome(s)	Main findings
Hanrahan [**34**] Grade C	45 (mean age 83 [SD = 8.9] years; 78% female) patients with end-stage dementia enrolled in home-based and institutional hospice programmes, Chicago, USA.	Two-year prospective longitudinal study of utility of NHPCO guidelines to appropriately identify dementia patients eligible for hospice care. All patients followed-up for 6 months.	Level of deterioration (FAST), common medical complications of dementia (physician survey), non-terminal significant co-morbidities (cardiac, circulatory, neurological, and renal functioning), presence/absence of aggressive care (tube feeding, antibiotics, Foley catheters).	Survival time in days between hospice enrolment and patient death or, for survivors, the end of the study.	Mean survival time of patients who were FAST stage 7C at admission (n = 24; 56%) was 4.1 months (median 27 days); 71% died within six months. Non-ordinal patients ($n = 20$; 44%) survived significantly longer ($P < 0.01$) for an average of 10.9 months. The use of Foley catheters decreased survival time independent of FAST scores ($P = <0.03$). The results confirm usefulness of NHPCO guidelines in identifying a sub-group of dementia patients with a survival time of ≤6 months.
Marquis [**35**] Grade B	142 (mean age 65 [SD = 9] years; 18% female) stable COPD patients recruited as they entered a 12-week out-patient pulmonary rehabilitation programme, Canada.	Prospective cohort study to test hypothesis that a reduction in $MTCSA_{CT}$ is a better predictor of mortality in COPD patients than low BMI. Patients were followed-up for a mean of 41 (±18) months up to the time of data analysis in November 2001.	Age, sex, anthropometric measurements (body weight [BMI]; height; midthigh circumference, quadriceps skinfold thickness), CT of thigh ($MTCSA_{CT}$), lung function tests (DL_{CO} [% predicted]; FEV_1 [% predicted]; FEV_1 [L]; FEV_1/FVC [% predicted]; FVC [L]; FVC [% predicted]; TLC [% predicted]); arterial blood gases ($PaCO_2$ [mm Hg], PaO_2 [mm Hg]); exercise tests (peak workrate [% predicted]; peak workrate [watts]).	All cause mortality during the study period.	25 (17.6%) patients died during the study period. In the univariate model age, sex, FEV_1 % predicted, BMI, thigh circumference, $MTCSA_{CT}$, peak workrate % predicted and PaCO2 were associated with mortality ($P < 0.15$). In the multivariate model only $MTCSA_{CT}$ ($P < 0.0008$) and FEV_1 % predicted ($P < 0.01$) were significantly associated with mortality. A repeat multivariate analysis with $MTCSA_{CT}$ and FEV_1 % predicted dichotomised found that $MTCSA_{CT}$ <70 cm^2 was associated with a fourfold (95% CI, 1.52–8.09) increase in mortality, independent of other variables ($P = 0.004$).
Nishimura [**36**] Grade A	227 (mean age 68.0 [SD = 7] years; 10% female) COPD patients attending 1 of 20 university and city hospitals in the Kansai area of Japan.	Prospective multi-centre longitudinal survey to compare the effects of the level of dyspnoea with disease severity (evaluated by airways obstruction) on mortality in COPD patients followed up for 5 years.	Age, sex, smoking status, presence/absence of chronic bronchitis (cough and sputum lasted 3 months for >1 year), lung function tests (DL_{CO2}/ VA [ml/min/l/mm Hg]; FEV_1 [% predicted]; FEV_1 [L]; FEV_1/ FVC [% predicted]; VC [L]; RV/TLC [% predicted]), arterial blood gases ($PaCO_2$ [mm Hg]; PaO_2 [mm Hg]), dyspnoea (modified MRC 5-point grading system).	Effects of the level of dyspnoea (modified MRC 5-point grading system) and disease severity (based on the staging of disease severity in the ATS Guideline) on 5-year survival rate of COPD patients.	Of the 183 patients available for follow-up 42 (23%) patients were stage I (FEV_1.50% predicted), 59 (32%) were stage II (FEV_1 35–49% predicted) and 82 (45%) were stage III (FEV_1 <35% predicted). Staging of disease severity did not significantly effect 5-year survival ($P = 0.08$). When classified by level of dyspnoea 67 patients (36%) were grade II, 87 (48%) were grade III, 26 (14%) were grade IV, and 3 (2%) were grade V. The level of dyspnoea was significantly correlated with 5-year survival ($P < 0.001$).

continued

Table 1. *continued*

Oga [37] Grade A	150 male (mean age 68.7 [SD = ±6.9] years) COPD out-patients attending the Kyoto University Hospital, Japan.	Prospective cohort study of relationship between exercise capacity, health status and mortality in stable COPD patients followed-up for 5 years.	Age, smoking status, BMI, lung function tests (pre-bronchodilator FEV_1 [L]; pre-bronchodilator FEV_1 [% predicted]; post-bronchodilator FEV_1 [% predicted]; DL_{CO} [% predicted]; DL_{CO}/VA [ml/min/l/mm Hg]); exercise test (peak VO_2 [ml/min]), health status (CRQ, SGRQ, BPQ).	Mortality in COPD patients after 5 years.	After 5 years 31 of the 144 patients available for follow-up had died. Univariate analysis showed that the SGRQ total score ($P = 0.00017$) and the BPQ ($P = 0.0044$) were significantly associated with mortality. In the multivariate model peak VO_2 uptake ($P < 0.0001$) and SGRQ total score ($P = 0.012$) were both predictive of mortality independent of age and FEV_1. Stepwise multivariate analysis revealed that peak VO_2 ($P < 0.0001$) and age ($P = 0.0024$) were the most significant predictors of mortality

ADL, activities of daily living; APACHE, acute physiology, age, chronic evaluation; ATS, American Thoracic Society; BMI, body mass index; BPQ, breathing problems questionnaire; CI, confidence interval; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CPS, clinical prediction of survival; CRQ, chronic respiratory disease questionnaire; DL_{CO2}, diffusing capacity for carbon dioxide; DL_{CO}, diffusing capacity for carbon monoxide; ESLD, end-stage liver disease; FAST, functional assessment staging; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; FiO_2, fractional oxygen uptake; GDS, Global Deterioration Scale; KPS, Karnofsky Performance Scale; MRC, Medical Research Council; $MTCSA_{CT}$, mid-thigh muscle cross-sectional area obtained by CT scan; MSOF, multiple system organ failure; MSQ, Mental Status Quotient; NHPCO, National Hospice Organisation; OARS, Older Adults Resources and Services Instrument; PaP Score, Palliative Prognostic Score; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen; RV, residual volume; ROC, receiver operating characteristic; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire; SUPPORT, study to understand prognoses and preferences for outcomes and risks of treatment; TLC, total lung capacity; VA, alveolar ventilation; VC, vital capacity; VO_2, oxygen uptake.

clinical and two laboratory items but the main contributor to the total score is the clinicians' prediction of survival (CPS). About 60% of the patients in Glare *et al.*'s study had very poor performance ratings (KPS = ≤20) and a CPS of <1 month. At the end of the study, >60% of all patients had died within a month; agreement between CPS and actual survival was moderate ($\kappa = 0.59$). These results offer preliminary evidence that the PaP score can be used to predict 30-day survival in non-cancer as well as cancer patients.

Walter *et al.* have developed an index to estimate risk of 1-year mortality in all elderly adults aged ≥70 years discharged from hospital [**31**]. This (grade A) study reported that the presence or absence of six risk factors (see Table 1) was significantly associated with increased risk of 1-year post-hospital mortality. Importantly, after adjustment for functional status and comorbidity, age did not improve the predictive power of the index. This bedside risk-scoring system may offer clinicians quantitative guidance for decision making, including appropriateness of palliative care for older adults with life-threatening non-malignant disease.

Predicting survival in dementia patients

Three studies (one grade B, two grade C) evaluated the accuracy and usefulness of medical guidelines (based on the NHPCO's recommendations) to determine prognosis in hospice-based patients with dementia [**32–34**]. The level of evidence in these studies ranged from poor to moderate. They report that presence of advanced dementia (equal to stage 7C of the FAST scale), along with history of medical complications and dependency of ADLs are prognostic for ≤6 month survival in dementia patients referred to home or hospice programmes. Further validation is needed to assess the prognostic value of these variables in the general dementia population.

Prognosis in COPD

Three studies (two grade A, one grade B) evaluated correlates of longer-term mortality (≤5 years) in relatively stable, community-based COPD patients [**35–37**]. Their findings suggest that, in addition to age and FEV_1, MTCSA, level of dyspnoea, peak VO_2 and SGRQ total score should be evaluated in determining long-term prognosis in community-based and stable COPD patients aged 65 years and older. These prognostic measures may help clinicians avoid inappropriately early referral to specialist palliative care for a subset of community-based COPD patients, but further research is needed to assess their acceptability and feasibility in routine clinical practice.

Discussion

This systematic review summarises the results of 11 studies identified in the literature that met our inclusion criteria and which evaluated the ability of prognostic models and factors to predict survival in older adults with life-threatening, non-malignant disease. A number of general and disease-specific factors were found to be significantly associated with survival. The specific findings from the 11 papers can be generally split up by disease entity—dementia, CHF and COPD—although that was not our original aim.

Chief among the specific predictors of short-term survival in dementia were loss of ambulatory function and impaired speech—equal to stage 7C of the FAST scale. However, in the three studies that assessed survival in dementia patients, the weight of evidence presented was generally poor. Sample sizes were small and those patients whose disease progression was not linear could not be scored using the FAST scale, leading to a reduction in its sensitivity. For example, Luchins *et al.* [**33**] report that only about half of patients could be rated using the FAST scale. Additionally, the study samples were enrolled in hospice programmes and it is uncertain how accurate prognostic criteria recommended by the NHPCO would be in predicting survival in the general dementia patient population [**39**].

For COPD, reduced pulmonary function ($FEV_1 < 30\%$), arterial blood gas measures and cor pulmonale with pulmonary hypertension are established predictors of poor prognosis in severely affected patients [**40**]. However, in recognition that FEV_1 may not be the single most important evaluative parameter in non-hospitalised patients, a number of other, novel prognostic factors were identified. These included dyspnoea, muscle mass, health status and exercise capacity. The MRC dyspnoea scale is a measure of respiratory trauma, but Nishimura *et al.* show it to be more discriminatory than FEV_1 in assessment of disease severity and survival in COPD. The level of dyspnoea may thus be a useful adjunct to FEV_1 in clinical evaluation of COPD patients. Measures of systemic change are also associated with mortality. As with other chronic diseases, weight loss in COPD is common and characterised by preferential muscle loss. Therefore, muscle mass and not body weight may be a more important predictor of mortality, especially when obesity and fluid retention are clinically manifest [41]. In addition, Oga *et al.* showed that systemic measures of change in health status and exercise capacity may be as important as functional parameters in the multi-factor evaluation of relatively stable COPD patients. More specifically, on the basis of this review, the SGRQ is the health status measure of choice, whilst peak VO_2 is perhaps the preferred measure of exercise capacity over, for example, maximal work rate, which has been used in younger COPD patients [42].

For CHF, specific predictors of mortality included advanced age, LVEF <40%, arrhythmia and systolic hypotension. Additional variables identified were comorbidities of cancer, cerebrovascular disease, liver cirrhosis, COPD and dementia, and laboratory and clinical parameters. The prognostic model developed by Lee *et al.* appears to offer clinicians assistance in identification of heart failure patients at higher risk of mortality, but it has yet to be validated in the general, non-hospitalised population. In the UK at least, not enough is known about disease severity and prognoses in typical community-based populations with symptomatic heart failure, some of whom will be appropriate for palliative care [43]. As with COPD, differences between hospitalised and community-based patients should be acknowledged when determining short-term survival and appropriateness of palliative care in patients with CHF.

Of the generic measures reviewed, the prognostic index for elderly adults developed by Walter *et al.* may be useful for determining 1-year survival in older patients discharged from hospital. However, problems of recall, computation and a failure to associate this risk index with instructions for appropriate therapeutic or palliative care are likely to restrict its acceptance and use among clinicians [44]. By contrast, the PaP score does offer a degree of quantitative guidance about the appropriateness of immediate referral to palliative care. However, although the PaP score is a well-validated and simple measure of short-term survival in cancer patients, evidence of its accuracy in older non-cancer patients is only of moderate quality. Glare *et al.* pooled data collected from a small and highly heterogeneous palliative population that included trauma and AIDS patients [30]. In addition, the main component of the PaP score is the CPS. Clinical estimates of survival are known to be frequently inaccurate in cancer patients and particularly problematic in patients dying from causes other than cancer. The overall accuracy of the PaP score may be reduced when calculated by inexperienced clinicians and in cases of non-malignant disease with unpredictable death trajectories.

Limitations

Our initial aim was to identify studies that described tools or variables that might aid clinicians in assessing survival and appropriateness of specialist palliative care in elderly adults with life-threatening, non-malignant disease. Estimated survival is likely to form part of the assessment of appropriateness for palliative care and we have suggested that prognoses of 6 months or less may signify the most appropriate time for referral to specialist palliative care, but this cut-off may not be applicable in all cases. The results of the review may have differed greatly had the search strategy been designed to identify studies about prognoses alone—the literature on prognoses is large and we may have excluded or overlooked studies that described measures of survival in non-malignant disease. However, the studies reviewed present a set of potentially useful generic and disease-specific variables for assessing short- and long-term survival in three disease groups that have established, but unmet palliative care needs: dementia, COPD and CHF.

Epidemiological and prognostic studies that report significant associations are more likely to be published than those that fail to report positive findings [45] and the findings of this review may therefore be limited by publication bias. In addition, only two out of the 11 included studies fully described treatments given to patients, thus making it impossible to provide an unbiased assessment of the prognostic ability of all factors.

Recommendations

Compared with cancer patients, the end-of-life experiences of non-cancer patients are heterogeneous, reflecting the unpredictable nature of chronic, non-malignant disease [**46**, **47**]. Attempts to predict short-term survival and identify non-cancer patients appropriate for palliative care may therefore be, at best, impractical and, at worst, unrealistic. Indeed, basing criteria for referral to specialist palliative care solely on prognostic estimates may lead to the palliative care needs of some non-cancer patients with, for example, favourable prognoses, being overlooked. Linking the provision of specialist palliative care too closely with prognosis precludes the development of models of palliative care that are responsive to patients' needs at all stages of disease, from diagnosis through to the end of life [**48**].

However, uncertainty about the onset of palliation and time to death in older, non-cancer patients is, undoubtedly, compounded by problems of prognostication in this group. To some extent, this problem stems from clinicians' lack of training in prognostication [49], but it also relates to the need for simple, well-validated prognostic models with good calibration, inter-rater reliability and generalisibilty [50]. Specifically, this review has identified a need for research of the potential prognostic role of social as well as physical factors in older, non-cancer patients. Spiritual beliefs have also been shown to be predictive of clinical outcome in cancer patients but have yet to be investigated in non-cancer patients [51]. There is also an equally pressing need for research that evaluates best practice in the management of older, non-cancer patients. Some life-threatening non-malignant diseases may be more appropriately managed by mixed models of care that offer both active and palliative treatments right up to the time of death. To understand this better we need research that addresses the impact of general and specialist palliative care on the physical and psychosocial health of non-cancer patients and their carers.

Conclusion

This systematic review identified 11 studies that aimed to evaluate prognosis in older adults with life-threatening, non-malignant disease. A number of general and disease-specific prognostic factors were identified but the heterogeneity of non-cancer patient populations and the unpredictable course of non-malignant disease compounds problems of prognoses in this group. No prognostic model presented in this review can be recommended for routine clinical use without further validation. Social and psychological factors have also not been well investigated and may play a part in the determination of survival and/or palliative status in non-cancer patients. Additionally, it is not known whether specialist palliative care is the preferred and most appropriate model of care for older, non-cancer patients. Intervention studies that assess the effect of all forms of palliative care on physical and psychosocial outcomes in non-cancer patients and their carers is needed.

Key points

- It is difficult to accurately predict ≤6 month survival in non-cancer patients—even the best models have poor discrimination.
- This difficulty probably reflects the unpredictable natural history of most non-malignant disease.

- There is a need for simple and well-validated prognostic models that enhance clinicians' own estimates of survival and offer guidance about future care strategies.
- Referral to specialist palliative care for older, non-cancer patients needs to be based on criteria other than survival alone, but better estimates of survival may facilitate decision making about appropriate palliative care.

Acknowledgements

The research was funded by a grant from the UK Department of Health (grant no: 0250026). The views expressed in this paper are those of the authors and not the Department of Health. No conflicts of interest are declared and no ethical approval was required.

References

The very long list of references supporting this review has meant that only the most important are listed here and are represented by bold type throughout the text. The full list of references is available on the journal website (www.ageing.oupjournals.org). Please see Appendix 5.

1. Higginson IJ. Palliative and terminal care. In Stevens A, Raftery J eds. Health Care Needs Assessment: Second Series: The Epidemiologically Based Needs Assessment Reviews. Abingdon: Radcliffe Medical Press, 1997.

3. Addington-Hall J. Reaching out: specialist palliative care for older adults with non-malignant diseases. London: NCHSPCS, 1998.

5. Skilbeck J, Mott L, Page H, Smith D, Ahmedzai SH, Clark D. Palliative care in chronic obstructive airways disease: a needs assessment. Palliative Med 1998; 12: 245–54.

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: 1000–6.

7. Edmonds P, Karlson S, Khan S, Addington-Hall J. A comparison of the palliative care needs of patients dying from chronic respiratory diseases and lung cancer. Palliative Med 2001; 15: 287–95.

8. Field D, Addington-Hall J. Extending specialist palliative care to all? Soc Sci Med 1999; 48: 1271–80.

11. Farquhar M, Grande G, Todd C, Barclay S. Defining patients as palliative: hospital doctors' versus general practitioners' perceptions. Palliative Med 2002; 16: 247–50.

12. Christakis NA, Lamont EB. Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study. BMJ 2000; 320: 469–72.

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

14. Morita T, Tsunoda J, Inoue S, Chihara S. The palliative prognostic index: a scoring system for survival of terminally ill cancer patients. Support Care Cancer 1999; 7: 128–33.

15. Piravano M, Maltoni M, Nanni O *et al*. A new palliative prognostic score: a first step for the staging of terminally ill cancer patients. J Pain Symptom Manage 1999; 17: 231–9.

18. Alderson P, Green S, Higgins J eds. Cochrane Reviewers' Handbook. The Cochrane Collaboration, 2004. (http://212.49.218.203/newgenMB/WebHelpSpecific/handbook.pdf)

19. Khan KS, Riet G, Glanville J, Sowden AJ, Kleijnen J eds. Undertaking systematic reviews of research on effectiveness. CRD's guidance for those carrying out or commissioning reviews. CRD report number 4. 2nd edition, 2001. (http://www.york.ac.uk/inst/crd/report4.htm)

27. Knaus WA, Harrerll FE, Lynn J *et al*. The SUPPORT prognostic model. Objective estimates of survival for seriously ill hospitalised adults. Ann Intern Med 1995; 122: 191–203.

28. Fox E, Landrum-McNoft K, Ahong Z, Dawson NV, Wu AW, Lynn J. Evaluation of prognostic criteria for determining hospice eligibility in patients with advanced lung, heart, or liver disease. JAMA 1999; 282: 1638–45.

29. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure. Derivation and validation of a clinical model. JAMA 2003; 290: 2581–7.

30. Glare P, Eychmueller S, Virik K. The use of the palliative prognostic score in patients with diagnoses other than cancer. J Pain Symptom Manage 2003; 26: 883–5.

31. Walter LC, Brand RJ, Counsell SR *et al*. Development and validation of a prognostic index for 1-year mortality in older adults after hospitalization. JAMA 2001; 285: 2987–94.

32. Hanrahan P, Luchins DJ. Feasible criteria for enrolling end-stage dementia patients in home hospice care. Hosp J 1995; 10: 47–53.

33. Luchins DJ, Hanrahan P, Murphy K. Criteria for enrolling dementia patients in hospice. J Am Geriatr Soc 1997; 45: 1054–9.

34. Hanrahan P, Raymond M, McGowan E, Luchins D. Criteria for enrolling dementia patients in hospice: a replication. Am J Hospice Palliative Care 1999; 16: 395–400.

35. Marquis K, Debigaré R, Lacasse Y *et al*. Midthigh cross-sectional area is a better predictor of mortality than body mass index in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2002; 166: 809–13.

36. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airways obstruction in patients with COPD. Chest 2002; 121: 1434–40.

37. Oga T, Nishimura K, Tsukino M, Sato S, Hajro T. Analysis of the factors related to mortality in chronic obstructive pulmonary disease. Role of exercise capacity and health status. Am J Respir Crit Care Med 2003; 167: 544–9.

38. Stuart B, Alexander C, Arenalla C *et al*. Medical guidelines for determining prognosis in selected non-cancer diseases, 2nd edition. Arlington, VA: National Hospice Organization, 1996.

39. Volicer L. Hospice care for dementia patients. J Am Geriatr Soc 1997; 45: 1147–9.

40. Glare P, Christakis N. Predicting survival in patients with advanced disease. In Doyle D, Hanks G, Cherny N, Calman K eds. Oxford Textbook of Palliative Medicine 3rd edition. Oxford: Oxford University Press, 2004, 29–42.

46. Claessens MT, Lynn J, Zhing Z *et al*. Dying with lung cancer or chronic obstructive pulmonary disease: Insights from SUPPORT. J Am Geriatr Soc 2000; 48: s146–s53.

47. 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: s101–s9.

48. Ahmedzai SH, Walsh TD. Palliative medicine and modern cancer care. Semin Oncol 2000; 27: 1–6.

Received 3 September 2004; accepted in revised form 21 December 2004