2.4 Predicting survival in patients with advanced disease

Paul Glare and Nicholas Christakis

Introduction

Why the renewed interest in the importance of prognosis in palliative medicine?

The three great clinical skills in medicine are diagnosis, treatment, and prognosis. Prior to the turn of the twentieth century, prognosis was much more prominent than it is today. For example, the nineteenth century physician was esteemed if he could diagnose pneumonia, and in the absence of effective treatment, predict whether a patient was likely to succumb to the illness. As effective therapies for many previously fatal illnesses were discovered during the first half of the twentieth century, prognosis gave way to treatment as the core clinical skill accompanying diagnosis; increasingly successful therapies made details of the natural history of illness progression seem less relevant to the clinician.[1]

The rise of palliative medicine as the study of specialized care for patients with incurable illnesses has set the scene for a renaissance of prognostication as a clinical skill. But unlike the nineteenth century, where prognosis often involved acute illness in young adults, in palliative medicine, prognosis frequently relates to chronic progressive and ultimately fatal diseases and co-morbidities in the elderly. The reasons for prognostication in incurable disease that have been put forward are therefore not to predict recovery but:

- to provide patients and their families with information about what the future is likely to hold so that they can set their goals, priorities, and expectations of care;[2–6]
- to help patients develop insight into their dying;[5]
- to assist clinicians in their decision-making;[7]
- to compare like patients with regard to outcomes;[8]
- to establish patients' eligibility for care programmes, including timely referral to hospice programmes;[7,9]
- to establish patients' eligibility for clinical trials;
- for policy making with respect to appropriate resource utilization and allocation of support services, for example, frequency of contacts if home care is proposed; and[5–7]
- to provide a common language for health care professionals involved in end of life care.

It is apparent that some of the foregoing items are more relevant before referral to palliative care services while others are more relevant after referral.

Prognosis in 'terminal' disease

Prognosis is a generic term related to predicting any health outcome. When it is related to a potentially life-threatening illness such as cancer, it is closely related to diagnosis, in that the same clinical and pathological factors which are used to make a diagnosis are also relevant to the prognosis. Most of the literature dealing with prognosis in cancer concerns factors that influence the probability of cure. For example, in the case of early breast cancer, tumour size and grade, oestrogen receptor status, age, menopausal status, and axillary lymph node involvement are used to stage the disease and these have prognostic import with respect to standard oncological outcomes that include, but are not restricted to, survival: the length of time until disease recurrence, median survival, and the percentage of cases still alive at standard oncological time points, such as 5 and 10 years. Different treatments are also compared with respect to their impact on survival: for example, after their initial surgery and radiotherapy, post-menopausal women with breast cancer and positive nodes have less local recurrence and a 10.9 per cent reduction in the probability of dying at 10 years if they are given adjuvant hormone therapy with tamoxifen.[10]

In patients with incurable advanced cancer, the diagnostic, pathological, and treatment differences that determine survival in early stage disease are typically less relevant. Moreover, because this is a very heterogeneous group of patients with respect to tumour type, these factors are replaced by different clinical and treatment factors which are not related to the principal diagnosis but to broader syndromic manifestations of terminal illness: physical dependency, the anorexia–cachexia syndrome, lymphopaenia, poor quality of life, and so on. Nevertheless, some patients with incurable cancer can be on the brink of death while others are relatively healthy and have months or even years to live.

In other eventually fatal illnesses, like COPD and cardiac failure, disease-specific factors like arterial blood gas levels and left ventricular function are more relevant to prognosis. Non-specific factors like symptoms (e.g. dyspnoea at rest), functional level, and quality of life are still very relevant nevertheless.

Different death trajectories

A fundamental issue affecting the prediction of survival is the possibility of prototypal death trajectories (Fig. 1).[11,12] The extent to which such hypothesized prototypal death trajectories actually occur is not fully understood at present, nor is it clear what fraction of patients with each of several different kinds of illness show each of these, or other possible, trajectories.

Nevertheless, it is clear that there is little role for palliative care in sudden death, other than to offer bereavement follow-up (Trajectory a). The prototypal cancer death involves a relatively predictable decline in health status over a period of weeks or months (Trajectory b). This is the bailiwick of palliative care and the pattern of deterioration for which traditional palliative care services such as hospices are best designed. This inexorable decline occurs because the cancer–cachexia syndrome seems to be the final common pathway of most solid tumours.[13] While the causes of death in cancer patients are quite diverse and often ultimately result from acute, potentially reversible problems with variable outcomes, such as infection,[14] in most cases the underlying tumour precipitates the cause of death (with anorexia–cachexia syndrome and coma as the final common pathway—see section on symptoms).

In chronic progressive illnesses other than cancer, different death trajectories may apply and two main ones have been described. One is the

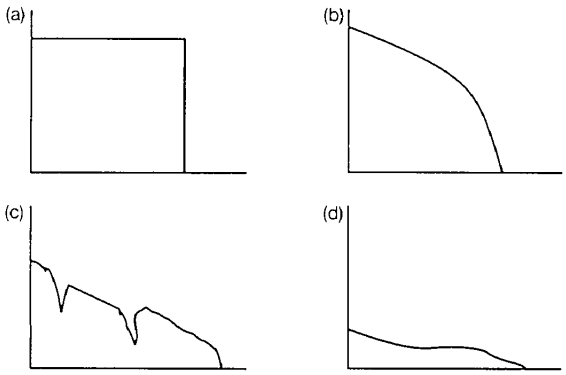

Fig. 1 Different death trajectories—health status is on *y* axis, time on *x* axis (adapted from refs 11 and 12). (a) Sudden death; (b) Typical cancer death; (c) Typical death from end-organ failure (e.g. CHF, COPD, or HIV/AIDS); (d) Typical death from dementia.

slow decline punctuated by acute crises from which the individual recovers to—or close to—the prior health state until the final crisis occurs that cannot be, or is not, treated (Trajectory c). The AIDS-related death and most end-organ failure deaths [e.g. chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF)] are typical of this pattern. The other is long-term languishing in a very poor health state culminating in death at some unpredictable time following no obvious event, typical of the post-stroke or Alzheimer's death (Trajectory d). Such possible differences in death trajectory may make the role of palliative care harder to define in non-cancer diagnoses.

Some authors have tried to make a distinction between advanced cancer (when disease is widespread but there is still some realistic hope of controlling it, if not curing it) and terminal cancer (when disease is widespread and there is no realistic way of controlling it) and to thereby determine the length of the so-called 'terminal phase'. The following durations of the terminal phase have been calculated:

Author	Country	Year	Survival (days)	
			Mean	Median
McCusker[14]	United States	1984	94	45
Vigano[15]	Canada	2000	175	107
Llobera[16]	Spain	2001	99	59

Thus it can be seen that the median duration of the terminal phase of cancer is around 2–4 months.

Different cultural aspects of prognostication at the end of life

The importance that physicians place on predicting survival at the end of life will be strongly influenced by socio-cultural factors. In his book, the *Nature of Suffering*, Cassell reminds us that in Hippocrates' day, the physician who was a good prognosticator was most highly esteemed amongst his colleagues.[17] By contrast, many religious traditions insist that only God or Allah knows the hour of an individual's death.

In liberal, pluralist Western societies physicians are generally willing to discuss the prognosis, along with the diagnosis and treatment, of a life-threatening illness. In many non-English speaking cultures, such discussions have traditionally been avoided, although this situation may be gradually changing.

The traditional palliative medicine approach to prognostication

In the past, prognostication—both foreseeing and foretelling—has received little attention within palliative medicine. Typically, some aspects of prognostication are brought out during palliative medicine training in Britain, the United States, and Australia. The main emphasis of training is good clinical decision-making in the context of far-advanced disease. Most stress is given to the necessity of taking into account the natural history of eventually fatal illnesses (without ever being taught much explicit content of that) and predicting the future consequences of a therapeutic act/omission, rather than predicting length of survival. Nevertheless, it is generally recognized that patients and (more often) families would sometimes ask for a prognosis, and it is a fundamental principle that the patient's goals, priorities, and expectations are what drives decision-making, not disease-related issues. The palliative medicine trainee in Britain is typically taught not to formulate a prognosis in terms of a specific amount of time,[18] but rather to offer a timeframe that has been supposed to be meaningful to the patient/family: namely, hours rather than days, days rather than weeks, weeks rather than months, and so on. For example, a 'weeks–months' prognosis formulated in November would be communicated as 'likely to make it to Christmas but unlikely to still be here for Easter'. Much prognostic importance is attached to interpreting how quickly the disease seems to have been progressing. A similar pattern has been documented in the United States.[19]

In terms of disclosing the prognosis, trainees are explicitly and implicitly taught to only disclose the formulated prognosis when it is requested and then to give a frank disclosure.[19] Much is made of the prognostic accuracy of the experienced nursing staff in the hospice unit regarding when an imminently dying patient would finally die, and the phenomenon that individuals very close to death would 'hang on' until they achieved closure. There is some suggestion that patients can indeed postpone death until symbolically meaningful occasions.[20]

In the Department of Palliative Care at Royal Prince Alfred Hospital, Sydney, Australia, the proforma that was developed for the patient database asked the registrar/fellow completing the form to give a temporal estimate of the expected survival. This is expressed in terms of a time interval: less than 1 week (representing hours–days), 1–4 weeks (days–weeks), 4–12 weeks (weeks–months), or greater than 12 weeks (months–years). There was never any training in how to formulate these temporal estimates or any evaluation of the accuracy of these formulations, although recently this has been considered in a preliminary way.[21] Nor was it clear what the time was meant to represent. Was it the actual time this individual would live? Or the worse case scenario? Or the median survival of other patients like this? Or the 90 per cent survival of other patients like this? Or something else? In the United States, many hospices formally require admission paperwork to indicate expected survival but this is typically limited to checking a box that the patient has 'less than 6 months' to live. And again, the meaning of this statement has not been made clear, although physicians are very inaccurate.[2]

Deconstructing prognostication: foreseeing versus foretelling

There are two fundamental aspects to the clinical skill of prognostication. The first is foreseeing, that is, formulating the prediction. The second is foretelling, that is, communicating the prediction to the patient. Both foreseeing and foretelling can be studied and improved upon.[22]

Formulating a prognosis in the patient with advanced cancer

Prognostication is not restricted to predicting survival. Prognostication simply means predicting an outcome. In its strictest sense, it refers to 'the relative probabilities that the patient will develop each of the alternative outcomes of the natural history of his/her disease',[23] and so is amenable to sophisticated statistical analysis. In the case of kidney stones, for example, there are prognoses for spontaneous passage, need for surgery, response to other treatments, pain, and recurrence. In the case of cancer, there are prognoses for cure, restoration of function, recurrence, and response to therapy, pain, other symptoms, and death. In the case of palliative care, which is primarily concerned with eventually fatal illnesses, time to death is the key outcome of interest.

There are various ways the practicing clinician can rationally formulate a prognosis. One can rely on one's own experience, but this depends on having seen a lot of similar cases, having a reliable memory, and remaining dispassionate in one's assessments. One can consult an 'expert' in the field but this is not always feasible and is subject to the expert's own biases. One can consult a textbook, but as mentioned above, modern textbooks contain little or no information about the relative probabilities of outcomes of interest. One can employ validated, published algorithms of variable ease of use.[24–26] Finally one can do an electronic search of the medical literature, but again there have been few studies or systematic reviews done to date, although this is changing for survival prediction, especially in patients with advanced cancer.[27]

As with all research, the quality of the methodology of prognostic studies and the way it is reported has improved enormously over the past

Table 1 Characteristics of well-designed studies to evaluate the association of prognostic factors with survival[81]

There is a well-defined study population
An inception cohort design is used
The prognostic factors selected for study are appropriate and clearly defined
The sample size is adequate for the study to have sufficient statistical power
The end point is clearly defined
There is completeness of follow-up
The data analysis is appropriate to test the association between the study factors and survival, using the appropriate statistical tests
There is a measure of agreement between the predicted and actual survival
The definition of accuracy is explicit and appropriate

20 years. Several authors have attempted to review the literature on prognostication in patients with terminal illness and each has commented on the methodological weaknesses—and difficulties interpreting—the studies, especially the older ones.[3,27,28] Well-designed studies to evaluate the association of prognostic factors with survival need the characteristics shown in Table 1.

Clinical predictions of survival

The classic paper on clinicians' estimation of survival (CES) in terminal cancer was published in the British Medical Journal in 1972. (It is perhaps the ultimate irony that, according to the footnote at the end of the BMJ paper, the Parkes study was planned and initiated by the late Dr Ronald Welldon shortly before his own unexpected death in 1969.) In that study, patients with a cancer diagnosis admitted to St Christopher's Hospice for 'terminal care' were studied.[29] Referring doctors (GPs or hospital staff) at the time of referral made predictions of individuals' duration of survival (in weeks). Hospice medical and nursing staff also made predictions at the time of admission. Although most patients died within 12 weeks, the predictions of survival showed little relation to actual length of survival. Moreover, greater than 80 per cent of the erroneous predictions were in the overly optimistic direction (often out by a factor of 2 or more).

Subsequently there have been close to a dozen studies of CES in advanced cancer with varying types of predictions by doctors and other health care professionals of varying experience in terminal care.[2,5,6,15,16,30–37] The diversity of study designs used makes it hard to be certain how accurate clinical predictions are. Most series used so-called *temporal* predictions of survival, expressed in terms of the actual time to be lived by the individual patient, as an ordinal variable (i.e. actual number of days or, more usually, weeks) and these are the least accurate and generally overly optimistic (see Table 2).

Other studies have expressed survival duration as a probability, asking the estimator to state the probability that the patient would survive to a certain time point (e.g. what are the chances that the patient survive 2 months or less, 6 months or more, a year or more?). Others have asked the estimators to provide upper and lower estimates of survival, or to give the smallest interval that would include 90 per cent of deaths of similar patients. Still others have asked estimators to put patients into temporal groups. These last studies hint that physicians may be less prone to error if prognosis is elicited this way.[5,15,30,33,34,36] For example, when asked to decide if individual patients had more or less than a year to live, doctors and nurses assigned more than 1000 hospitalized cancer patients to the correct survival category in more than 75 per cent of cases, and were as likely to over-estimate as under-estimate survival.[33] In another study, two physicians had an accuracy of 60 per cent in predicting whether hospice patients would survive 4 weeks or not.[34] Table 3 provides some illustrative ways that prognoses might be elicited from estimators, with answers that are denominated in different units. The inaccuracy of temporal prognostication has been confirmed in our own systematic review of these studies which is evaluating more than 1500 temporal prediction-actual survival dyads.[38] The heterogeneity of the studies is high, making formal meta-analysis impossible but the pooled results show that CES consistently over-estimates survival, by 45 per cent in general. CES were correct to within 1 week of actual survival (AS) in only 25 per cent cases, and over-estimated AS by at least 4 weeks in 27 per cent. There was increasing variability in AS as CES increases. Nevertheless, although the level of agreement between CES and AS was low (weighed kappa 0.36), they were highly correlated, with $R^2 = 0.51$ for log transformations of both (Fig. 2).

Aside from the issue of whether different ways of eliciting prognoses are more or less accurate, there are other questions to ask about CES:

- *Are repeated estimates more accurate?* In the original Parkes study, doctors were actually less accurate a week later. Subsequently, several investigators have found that doctors' ensuing predictions on the same patients correlate more strongly with survival than their initial ones.[5,37,39]
- *Is there a 'horizon effect'?* Prognosis has a dynamic quality and may change (becoming more or less certain) as time passes. Whether CES are more accurate in those patients who are closer to dying has only been studied to a limited extent. In one study where patients had a median survival of 15 weeks, physicians were most likely to be correct (positive predictive value 74 per cent) when predicting a short survival (≤2 months), but they only predicted this in a small number (31 per cent) of the patients who actually survived less than 2 months.[15] Data from a study of more than 500 terminally ill patients (median survival 24 days) referred to hospices in Chicago, IL, in whom their own physicians were asked to make prognostic estimates, suggest that the extent of prognostic error varied depending on both observed and predicted survival, as shown in Table 8.[2] Because physicians were in general so optimistic in their estimates, the longer the *observed* survival, the lower the error. Conversely, the longer the *predicted* survival, the greater the error.
- *Does discipline make a difference?* In the Parkes paper, no significant differences were found between the accuracy of predictions made at referral by GPs, by hospital doctors, by hospice doctors on the day of admission, or by ward sisters and senior nurses at the same time. Several subsequent studies have mostly found no differences in the prognostic abilities of health care workers from different disciplines, although the numbers of prognosticators were usually small.[2,5,15,16,32] One recent British study found that while doctors were the best initial predictors, nurse auxiliaries became very accurate in the last few days of life ($r = 0.98$), presumably because of the amount of time they spend with the patient.[37]
- *Does experience make a difference?* Table 1 suggests that doctors working in the terminal care field have improved their powers of survival estimation over the past 20 years. In one study, the correlation between CES by palliative care specialists and AS increased with clinician experience, and as a group these prognosticators made errors (using the Parkes criterion, i.e. actual survival = predicted survival ± 100 per cent) in only 30 per cent cases, although most errors were still overly optimistic.[6] In the Chicago hospice study, only 20 per cent of the doctors' predictions were accurate (predicted survival = actual survival ± 33 per cent), 63 per cent were overly optimistic (predicted survival > actual survival + 33 per cent), and 17 per cent were overly pessimistic (predicted survival < actual survival − 33 per cent).[2] Multivariate modelling showed that most types of doctors are prone to error in most types of patients, although the greater the experience of the doctor the greater their prognostic accuracy. However, the stronger the doctor–patient relationship, the lower their prognostic accuracy. This suggests that the dispassionate, experienced physician is likely to be the most accurate prognosticator and raises the concept of seeking a 'second opinion' when a definitive prognosis is required.

Despite the inaccuracy of CES, it seems to be an important prognostic factor as it has been retained as an independent predictor of survival on multivariate analysis of a range of possible prognostic variables by several different investigators.[24,40] CES seems to depend more on the individual

Table 2 Association of clinicians' estimates of survival and actual survival in 12 studies

Author, country	Year	Prognosticator/s	Type of prediction	*n*	Median predicted survival (weeks)	Median actual survival (weeks)	Predictions that were accurate (%)	Predictions that were over-optimistic (%)
Parkes, United Kingdom	1972	Hospice doctors	Actual survival (weeks)	74	4.5	~3	8	66
Scotto, United States	1972	Oncologists	Actual survival (months)	178	NS	NS	NS	52
Evans, United Kingdom	1985	Terminal care support team	Upper and lower limits (days)	45	NA	~7	54	37
Heyse-Moore, United Kingdom	1987	Referring doctor	Actual survival (weeks)	50	8	2	4	88
Forster, United States	1988	University oncologist	Interval of likely death (weeks–months)	101	NA	3.5	NS	1[a]
Addington-Hall, United Kingdom	1990	Doctors and nurses	Live more or less than 1 year	1128	NA	17.5	75–83	12
Bruera, Canada	1992	Hospice physicians	Live more or less than 4 weeks	47	NA	4 (mean)	60	26–34
Maltoni, Italy	1994	Palliative care MD	Actual survival (weeks)	100	6	5	15	63
McKillop, Canada	1997	Attending physicians	Likely survival (months)	39	NA	~52	75	NS
Oxenham, United Kingdom	1998	Palliative care senior registrars	Date of death	30	NS	2.5	NS	NS
Vigano, Canada	1999	Oncologists	Actual survival (weeks–months)	233	15.3	14.5	52	NS
Christakis, United States	2000	GPs, internists, oncologists	Actual survival (weeks–months)	468	18	3.5	20	63
Llobera, Spain	2000	Oncologists, GPs	NS	200	NS	7.5	22–27	55–63

[a] 'seriously' over-optimistic, according to authors.

Notes: NA = not applicable, NS = not stated.

Table 3 Ways that prognoses might be elicited, with answers denominated in different units

'What is your best estimate of how long this patient has to live?'
'What is your best estimate of this patient's per cent chance of surviving for 7/30/90/180/360 days or more?'
'Of 100 such patients, how long would it typically be before 20/50/80 died?'
'How likely is this patient to live for 7/30/90/180/360 days or more?'
'Into which of the following categories is the patient's survival most likely to fall: 0–7, 8–30, 31–90, 91–180, or 181–365 days?'

perceptions of the person making the prediction rather than on 'common observations' (although it has been shown to correlate positively with performance status). Given that experienced physicians are more accurate prognosticators, it seems logical to ask if the prognosticators were willing to verbalize the thinking behind their estimates of life expectancy, this might provide useful insights into consideration and valuation of select clinical and social information.[41] A useful paradigm for conceptualizing prognostication, based on the ideas of MacKillop,[28] is shown in Fig. 3.

Performance status

Since CES does not seem to be very accurate, other ways of predicting survival duration in terminal cancer have been investigated. Various factors have been associated with survival, including demographics (age, gender, marital status), tumour-associated factors (primary site, histology, stage), performance status, symptoms, and psychological well being: almost 150 different variables that have been evaluated for their ability to predict survival.[27,42,43] Of all of them, performance status has been studied the most extensively and consistently shows an association with survival duration (see Table 4).

Ever since the development of the Karnofsky performance status (KPS) scale in the 1940s to assess the effects of chemotherapy on functional level, performance status has been recognized as a predictor of oncological outcomes, including survival (see Table 5). The first study to evaluate clinical variables as predictors of survival in advanced cancer evaluated the KPS scale. In that study, the authors primarily aimed to comprehensively establish the statistical properties of the KPS scale; in order to demonstrate its validity, the association of KPS scale score with other clinical variables including duration of survival was evaluated.[44] In a rehabilitation programme 152 cancer patients who had a predicted survival in the 3–12 months range were evaluated; 104 died during the follow-up period and it was found that that a poor performance status (KPS score <50) was associated with a short survival (although one patient with KPS score <50 survived beyond 6 months). While those with a better KPS score generally lived longer, the corollary was not true. A good KPS score (≥ 50) did not guarantee a long survival in this population, the KPS score rapidly dropped in the final 2 months of life. Many other authors have subsequently confirmed this association between KPS score and survival in advanced cancer.[5,6,13,16,27,45]

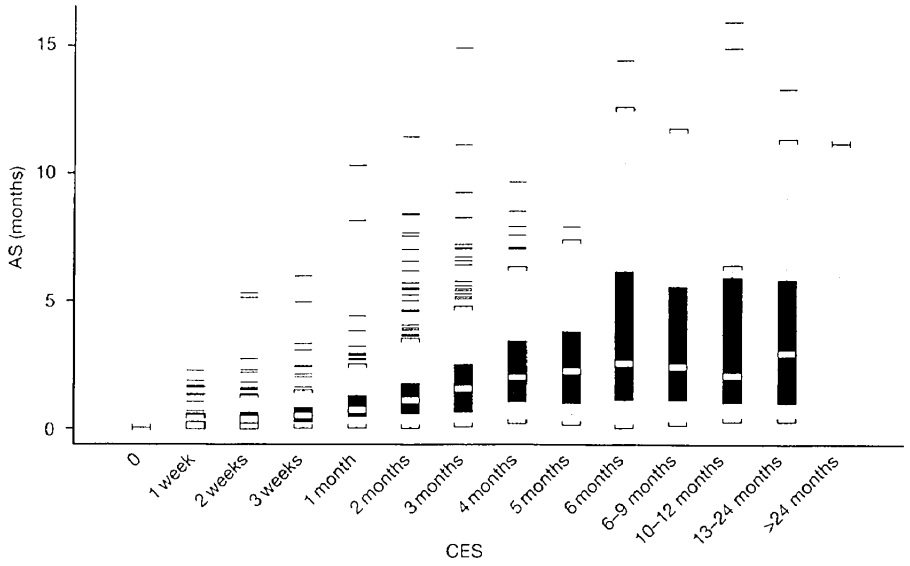

Fig. 2 Association between clinical prediction of survival and actual survival.[38] This is a plot of the differences between CES and AS. The boxes indicate the interquartile range (IQR) of AS, expressed in months. The middle bar is the median survival for the group. The whiskers are drawn to 1.5 times the IQR, which would represent the 99.65 percentile if the data were normally distributed (which they are not). Points beyond are drawn individually. It can be observed that when CES exceeds 6 months there is no predictive value in this measure. When CES is 6 months or less, AS equals or exceeds this estimate in no more than one in four patients. Thus the clinician's estimate is generally optimistic. The figure also demonstrates the increasing variability in AS as CES increases and the skewed distribution of AS, given the CES.

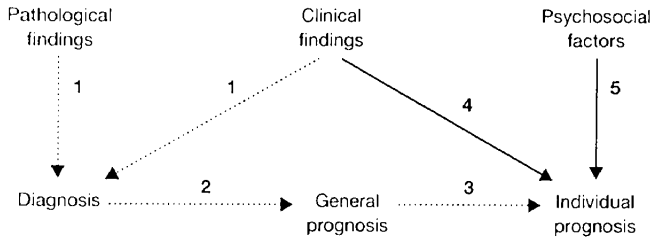

Fig. 3 Formulating a prognosis (adapted from ref. 27). Clinicopathological findings such as tumour histology, grade, and site/number of metastases lead to the diagnosis of the individual's disease. **1**, there is a general prognosis associated with this diagnosis, induced from the clinician's experience of previous patients with the same disease (expressed as 5-year survival rate, median survival, etc.); **2**, this general prognosis is then attributed to the individual patient; **3**, but needs to be modified according to other clinical findings such as performance status, symptoms, metabolic problems; **4**, and quality of life scores or other psychosocial variables; **5**, in patients with far-advanced/terminal cancer, factors **4** and **5** (solid lines) seem to be more important than **1**, **2**, or **3** (broken lines).

Table 4 The extent to which various clinical variables appear to be predicative of survival in patients with far-advanced cancer[40]

Variable	Number of positive studies[a]	Total number of evaluating studies	Strength of association
Poor performance status	14	14	Definite
Anorexia	8	9	Definite
CES	7	7	Definite
Cognitive failure	7	8	Definite
Dyspnoea	7	8	Definite
Dry mouth	5	6	Definite
Weight loss	4	5	Definite
Dysphagia	4	5	Definite
Primary site	5	10	Possibly yes
Pain	5	10	Possibly yes
Serum albumin	3	4	Possibly yes
Tachycardia	3	4	Possibly yes
Gender (male)	3	11	Possibly yes
Marital status	2	5	Probably not
Nausea	2	5	Probably not
Age	2	9	Probably not
Fever	1	4	Probably not
Anaemia	0	4	Probably not

[a] Positive on either univariate or multivariate analysis.

The National Hospice Study undertaken in the United States in the early 1980s involved over 1000 patients referred to hospice programmes, with an overall median survival of 37 days.[45] It found that the KPS score accounted for only a small amount of the variability in survival, but that it was highly statistically significant. In general, each increase in KPS level (e.g. from 10 to 20) added approximately 2 weeks to the remaining life span in this study. Furthermore, the KPS scores were used to group patients into survival risk classes (KPS score 10–20: median survival 2 weeks; KPS score 30–40: 7 weeks; KPS score ≥50: 12 weeks). Others have also shown that the KPS score can be used to stratify terminally ill patients for survival risk.[6]

It is unclear whether performance status is a better prognostic indicator than CES as neither has much positive predicative value for individual survival to a certain time point. One group found that the KPS score was more strongly correlated with survival than CES made at the initial visit,[5] while others came to the opposite conclusion (Maltoni, 1994). The latter study showed that the CES and KPS score were closely correlated ($r^2 = 0.37$). In other words, 37 per cent of the variation in the survival estimates was accounted for by changes in the performance status. It is possible that the greater accuracy of the survival estimates made by experienced clinicians

Table 5 KPS score and PPS

Percentage of normal performance status	KPS (Karnofsky definitions)	PPS					
		Ambulation	Activity level	Evidence of disease	Self-care	Intake level	Conscious
100	Normal, no complaints, no evidence of disease	Full	Normal activity	No evidence of disease	Full	Normal	Full
90	Able to carry on normal activity, minor signs or symptoms of disease	Full	Normal activity	Some evidence of disease	Full	Normal	Full
80	Normal activity with effort, some signs or symptoms of disease	Full	Normal activity with effort	Some evidence of disease	Full	Normal or reduced	Full
70	Cares for self, unable to carry on normal activity or do active work	Reduced	Unable normal job/work	Some evidence of disease	Full	Normal or reduced	Full
60	Requires occasional assistance, but is able to care for most of his needs	Reduced	Unable hobby/ house work	Significant disease	Occasional assistance necessary	Normal or reduced	Full or confusion
50	Requires considerable assistance and frequent medical care	Mainly sit/lie	Unable to do any work	Extensive disease	Considerable assistance necessary	Normal or reduced	Full or drowsy or confusion
40	Disabled, requires special care and assistance	Mainly in bed	Unable to do any work	Extensive disease	Mainly assistance	Normal or reduced	Full or drowsy or confusion
30	Severely disabled, hospitalization is indicated although death not imminent	Totally bed bound	Unable to do any work	Extensive disease	Total care	Reduced	Full or drowsy or confusion
20	Very sick, hospitalization necessary, active supportive treatment necessary	Totally bed bound	Unable to do any work	Extensive disease	Total care	Minimal sips	Full or drowsy or confusion
10	Moribund, fatal process progressing rapidly	Totally bed bound	Unable to do any work	Extensive disease	Total care	Mouth care only	Drowsy or coma
0	Dead	Dead					

compared with inexperienced ones is that they have learnt to take performance status into account when prognosticating, although this remains to be proven. Other investigators have confirmed this strong association between KPS score and CES, to the point that performance status dropped out of their survival models.[16,46] One problem with the KPS score is that, like other clinical scales, it is scored with varying degrees of inter-rated reliability. This improves with training and care is need when scoring it.[45] Patient-rated KPS scores provide independent prognostic information in addition to physician-rated KPS score.[13]

Other performance status ratings have not been investigated as extensively as the KPS score has. The ECOG scale has been shown to be predictive of survival in both advanced cancer[13] and terminal cancer.[47] ADL scores have also been associated with survival of cancer patients.[48] More recently, the Palliative Performance Scale (PPS), a modification of the KPS, has been developed by home hospice nurses in Canada as a new tool for measuring physical status in patients referred to palliative care services (see Table 5).[49] Initial testing of PPS showed that performance status in terminal cancer could be used for predicting various outcomes, including short-term survival. For example, patients admitted to a hospice unit with a PPS score of 10 all died in the unit, with an average survival of 1.9 days, while 56 per cent of those with a PPS score of 40 on admission died in the unit, with an average survival of 10 days. Full validation of the PPS is awaited, especially regarding whether it is more reliable than KPS score. Very similar results have been obtained with PPS for inpatients admitted to an Australian palliative care unit.[50] A Japanese group has shown that PPS scores are highly correlated with KPS scores (Spearman's $\rho = 0.94$) and tend to stratify patients admitted to a palliative care unit, who had an overall median survival of approximately 1 month, into three homogenous survival groups (PPS 10–20, median survival 6 days; PPS 30–50, median survival 41 days, and PPS 60–70, median survival 108 days).[51]

Symptoms

The onset of various symptoms has also been associated with poor survival in patients with far-advanced cancer. Classic work on this topic was first published by Alvin Feinstein in the mid-1960s, wherein it was argued that symptoms are a more robust indicator of cancer progression and hence prognosis than alternative pathology-based systems.[42] Following on from the findings in the early 1980s that performance status, while strongly associated with survival, did not have sufficient predictive accuracy to guide clinical decision-making in individual cases,[44,45] data from the National Hospice Study of patients after referral to hospice was used to determine whether symptom profile would supplement the accuracy of KPS score in accurately predicting survival.[52] This study showed that five of 14 symptoms evaluated were predictive of survival, namely, anorexia, weight loss, xerostomia, dysphagia, and dyspnoea. These symptoms supplemented prognostic information provided by performance status, especially for patients with better performance status. For example, patients with a KPS score greater than 50 and none of the five key symptoms had a median survival of approximately 6 months and a small (10 per cent) chance of living for 1.5 years; on the other hand, patients with similar performance status and all five symptoms had a median survival of only 2 months and a 10 per cent chance of living for 9 months. In patients with poor performance status, the results were as follows: patients with KPS score 10–20 with no symptoms have a median survival of 8 weeks while those with all the symptoms had a median survival of only 2 weeks.

The best association between survival and symptoms is for the symptoms associated with the anorexia–cachexia syndrome, namely, anorexia and weight loss (see Table 2). Generalized debility and weakness may be the terminal syndrome or pathway, prompting some to call cachexia the 'final common pathway' in patients dying from cancer.[13,53–55] While some studies have not found the symptom of anorexia per se to retain independent prognostic importance on multivariate analysis, other nutritional indices have inevitably been included in the regression models (e.g. weight loss, decreased serum albumin).

Subsequent to the National Hospice Study, several other authors have found dyspnoea to be a survival predictor.[7,24,47,56,57] There is also strong evidence for cognitive failure/confusion as a predictor of a poor survival in far-advanced cancer. A small study of patients admitted to a Canadian PCU was one of the first to explore the link between cognitive failure and poor survival. Patients with a mini-mental state examination score of less than 24, weight loss, and dysphagia had an increased risk of surviving for less than 4 weeks.[34] Somewhat surprisingly, neither anorexia nor dyspnoea was predictive of a short survival in that study. A number of others since,[16,35,56,58] but not all[47] have confirmed this finding.

Somewhat surprisingly, pain is not usually considered to be predictive of poor survival,[34,52] even though it is well known that pain increases in frequency and severity as cancer progresses. However, episodes of severe, uncontrollable ('unendurable') pain and breathlessness have been reported to be more common in the last few weeks of life.[59] Treatment with opioids does not have any impact on survival rate according to several groups of investigators.[47,60]

Quality of life

The relationship between symptoms and survival may be broadened to include the prognostic implications of measures of 'quality of life', in part because symptom distress scores have been recommended as a quality of life measure. A Canadian study of 434 patients with cancer who were within the first 6 months of diagnosis and had a median survival after enrollment of 300 days found that Symptom Distress Scores (SDS) were highly correlated with survival ($r = -0.49$).[61] In this study, fatigue, insomnia, frequent pain, and 'outlook' (sic) were the symptoms most commonly given high distress scores, but not anorexia (notably, weight loss, dysphagia, and dry mouth are not included in the SDS). Similar to performance status, low symptom distress scores did not guarantee long-term survival, but patients with high symptom distress all virtually had short survival times. There were significant differences in levels of symptom distress according to disease site.

A study of patients with hepatic metastases from colorectal cancer specifically showed that the physical symptom subscale score of the Rotterdam Symptom Checklist was the sole quality of life indicator (QOL) predicting survival.[62] In another study—of cancer patients with a median survival in excess of 2 years—a number of quality of life instruments were evaluated; on multivariate analysis, the physical symptom subscale score of the Memorial Symptom Assessment Scale—which averages the frequency, severity, and distress associated with 12 prevalent symptoms—was the only quality of life measure to independently predict reduced survival.[63]

The role of psychological factors in cancer survival has been controversial for more than two decades. A well-known study of over 350 newly diagnosed cancer patients conducted in the 1980s by Cassileth et al. found that 'the inherent biology of the disease [cancer] alone determines the prognosis',[64] and others have confirmed this finding more recently.[65] On the other hand, equally well-known studies like those by Greer and co-workers have identified psychosocial aspects of cancer survivors, such as the 'fighting spirit'.[66–68] Qualitative research of terminally ill cancer patients who were exceptionally long survivors showed that they adopted an 'active coping stance', characterized by: (i) belief in recovery, (ii) positive intentionality, (iii) a meaningful relationship with one doctor, (iv) an intense desire to stay alive.[69] Subsequently, a recent prospective study of psychosocial issues and breast cancer survival by Greer and colleagues found a significantly increased risk of death from all causes by 5 years in women with a high scores for depression and helplessness/hopelessness but there were no significant results found for fighting spirit.[70]

The relationship between survival and patient-related quality of life has been examined for advanced cancer in the oncology literature, and there is some evidence of an association. A significant association has been reported between patient-rated well being and survival time in women receiving treatment for advanced breast cancer,[71] and patient's perception of well being, measured by the Functional Living Index-Cancer (FLIC) instrument (a patient self-rated, cancer-specific QOL questionnaire) is more important in predicting survival in advanced lung cancer than other predictors like KPS score or weight loss.[72] Patients with high FLIC scores lived twice as long (6 months) as those with low scores (3 months). In patients with metastatic melanoma, various measures of QOL (Spitzer QLI, VAS for mood, appetite, and global QOL) have also been shown to be independent predictors of survival, along with KPS score and liver secondaries.[73]

More recently, global QOL scores measured using the EORTC QLQ C30 has been shown to be a strong prognostic indicator in patients with inoperable lung cancer, along with weight loss.[46] In the univariate analysis, a number of QOL subscales, symptoms (anorexia, fatigue, and dyspnoea), and performance status were significant, but dropped out in the multivariate analysis. Shadbolt has found that the global health status item at the beginning of the SF-36 is the best predictor of survival in patients with advanced, but not terminal, cancer.[74]

QOL has not been looked into much in patients with far-advanced disease after referral to hospice/palliative care services. Furthermore, measuring QOL in patients with terminal cancer is fraught with difficulties: (i) the usual QOL definitions and tools are not very applicable in dying patients, (ii) short survival and poor cognitive function makes QOL data difficult to collect, and (iii) the use of ratings by proxies has only limited value.[75]

Nevertheless, there has been some attempt to examine this question. The Spitzer Quality of Life Index (SQLI) has been evaluated for its ability to reduce prognostic uncertainty.[33] In patients estimated to live less than 1 year, there was a trend for those with a low SQLI score to be more likely to die within 6 months than those with a high SQLI. However, the individual patients' scores were not strong predictors of 6-month survival. For example, while 86 per cent of patients who died within 6 months had an SQLI score of less than 7, 65 per cent of those with an SQLI less than 7 were still alive at 6 months.

A validated Italian QOL questionnaire designed for use in hospice/palliative care, the Therapeutic Impact Questionnaire (TIQ), uses four-point Likert scales to rate four major components of QOL—physical symptoms, function, psychological state, and family and social relationships. Global well being is also evaluated. Of all the data provided by TIQ, only the patient-rated perception of cognitive function and global well being showed independent prognostic value. Patients had median survivals of 137, 50, and 17 days for impairment of neither, one, or both scales, respectively.[58]

The association between QOL and survival raises the same issues as with any other statistical association: causality, that is, does the patient's QOL actively influence the natural history of the disease and therefore the survival, or is the QOL merely a reflection of the severity of the illness, progressing inexorably towards death? This issue has been controversial for more than two decades, and needs well-designed clinical trials of interventions that improve quality of life to answer it. Other non-medical factors that influence survival include marital status and socioeconomic status. Marital status has been shown to modify the effect of QOL on survival in cancer patients.[72]

Biological parameters

It is well established that biological parameters are associated with survival of patients with early-stage cancer undergoing treatment. This observation includes both complex biological parameters, such as pathological grade and tumour receptor status, and simple biological parameters such as sodium, albumin, and lymphocyte levels.[76] For example, it has been recognized for 20 years that hyponatraemia is a predictor of a poor outcome

in lung cancer, and this was the first biological variable to be evaluated with respect to far-advanced cancer.[32]

Interest in biological parameters has gradually increased over the past 10 years. An Australian study in the early 1990s found a single biological parameter—elevated serum bilirubin—to be one of only four diverse clinical parameters that were predictive of survival on admission to a palliative care unit.[47] An Italian group has done the first large multicentre study of simple biological factors in far-advanced cancer.[77] They collected blood and urine in 530 patients from 22 palliative care centres who had a median survival of 32 days. They looked at various haematological and hepatic synthetic parameters, parameters that they hypothesized to be relevant. Specifically, they evaluated haemoglobin, white blood cell (WBC) count, and differential percentages (but not platelets), transport iron, transferrin, pseudocholinesterase, serum albumin, and proteinuria. They did not evaluate serum electrolytes, liver function tests, or serum calcium, all of which have been found to be important in other, smaller series. Most patients had abnormal values, except for the neutrophil, basophil, monocyte, and eosinophil percentages. Univariate analysis of survival found that the following were all associated with reduced survival: high total WBC, high neutrophil percentage, low lymphocyte percentage, low serum pseudocholinesterase, low serum albumin, and elevated proteinuria. On multivariate analysis, only high total WBC and low lymphocyte percentage retained independent prognostic significance.

Other parameters that have been evaluated include low serum albumin—for which the evidence is conflicting[40,47]—and elevations of serum alkaline phosphatase, lactate dehydrogenase, and C-reactive protein.

Prognostic scores/models

From all of the foregoing, it appears that there is the potential to combine various simple clinical and laboratory factors which are easily evaluated and measured in terminally ill cancer patients to provide physicians with accurate information about prognosis of the type '*x* per cent chance of surviving *y* days'. However, the concept of group probabilities—statistical relations between disease factors and outcomes—verges on anathema to many professionals within palliative care. The philosophical basis of palliative care focuses on understanding the patient as a person, the uniqueness of their suffering, and the clinician's personal interaction with the patient and their family, carefully avoiding anything that dehumanises the individual.

Nevertheless, although individuals exhibit unique features, clinicians cannot avoid making predictions about outcomes. Research commencing within the field of clinical psychology has shown that in general actuarial (statistical) methods are superior to clinical judgement in predicting human behaviour and other outcomes.[78] Actuarial judgement uses empirically established relationships between data and the condition or event of interest. Throughout clinical medicine, simple scoring systems, such as the Glasgow Coma Scale and the Killip Class of myocardial infarction, have proved useful. In cancer medicine, both physiological and psychological factors have been investigated for their ability to compare the accuracy of estimation of survival time. The parameters used for predicting 5-year survival rates in patients with earlier stages of cancer, such as primary site, stage of disease, clinical presentation and history, number of metastases, and location of metastases are generally not useful for predicting survival time as death approaches (see Fig. 3). Instead, several attempts have been made to combine one or more of the factors known to predict survival in the terminally ill (performance status, symptoms, quality of life, biological parameters) into a parsimonious mathematical model that can be used at the bedside to improve CES. The fact that actuarial judgement is more accurate than clinical judgement in advanced cancer is undoubtedly related to the fact that the underlying tumour precipitates the cause of death in the majority of cases making the final common pathway of the anorexia–cachexia syndrome so predictable (i.e. Trajectory B), and it has been recognized since the 1980s that poor performance status, nutritional symptoms like anorexia and weight loss, and the associated metabolic derangement constitute a 'terminal cancer syndrome'.[53,79]

Attempts to develop prognostic models for advanced cancer have been based on similar models in early-stage cancer where, for example, 61 biological variables were assessed for their prognostic value prior to commencement of chemotherapy in 400 patients with small-cell lung cancer.[75] Multiple regression analysis revealed that only tumour stage, KPS score, and four biochemical variables (serum sodium, bicarbonate, alkaline phosphatase, and lactate dehydrogenase levels) were important. Combining these six factors into a simple scoring system—the so-called 'Manchester Index'—the authors were able to accurately distinguish patients belonging to three different prognostic groups, the best of which contained all long-term survivors whereas the bad prognostic group contained no patient surviving greater than 1 year.

In patients with far-advanced cancer, many studies have developed multiple regression models to determine the association between prognostic factors and survival, but few have tested the predictive accuracy of their final models, a key step in prognostic model building.[80–82] Some of the better-developed ones are discussed in greater detail here.

National hospice study life table[52]

Using data from the US National Hospice Study of hospice referrals in the 1980s, these investigators looked at combining performance status—in this case KPS score—and symptoms. As mentioned previously, a poor KPS score ($\leq$50) is associated with poor survival, although better performance status (KPS score $\geq$50) does not guarantee good survival. Using these data and statistical modelling, the investigators found that the presence or absence of certain key symptoms was able to differentiate the patients with better performance who had short and long prognoses. Five out of 14 symptoms collected in the data set were identified as being predictive of poor survival: anorexia, weight loss, dysphagia, dry mouth, and dyspnoea. In patients with KPS scores greater than or equal to 50 and none of these symptoms, the median survival was 6 months; if all the symptoms were present it was only 6 weeks. If some were present, the prognosis was intermediate and depended on which of the combination were present. On the other hand, for patients with a very poor performance status (KPS score 10–20), symptoms were less important: if none were present, the median survival was 6 weeks; if all the symptoms were present it was 2 weeks. What makes this study particularly important is that the data from this analysis are presented in the form of a life table that can be easily read off by the clinician at the bedside. For example, a patient with a KPS score 30–40 and anorexia, weight loss, and dry mouth has a median survival of 59 days and a 10 per cent chance of still being alive in 258 days. Although internally validated on the source data set, these predictions are yet to be externally validated.

Australian study[47]

The Australian study of patients with far-advanced cancer requiring inpatient care used various clinical and physiological variables to predict survival. Multivariate analysis of 19 variables identified four that were independently prognostic: poor performance status (ECOG), hyperbilirubinaemia, hypotension, and, need for hospice admission at first clinic visit.

Patients were then categorized into 16 groups depending on which combination of these factors was present, and then these groupings were used to stratify patients into three survival groups: less than 1 month, 1–3 months, or greater than 3 months. The positive predictive value of the 16 groups for the stratification was low, ranging from 0.41 to 0.79 (median 0.5).

SUPPORT study[25]

This study was set up to identify deficiencies in the care of patients with eventually fatal illnesses (only some of whom had cancer) and who were hospitalized, making it difficult to compare with the other data about terminal cancer. Nevertheless, this study is relevant because it aimed to use accurate prognostic information as the cornerstone of improved

decision-making about end of life care in hospitals. Based on the APACHE system for prognostication in critically ill patients in ICU's, individuals' clinical and physiological parameters were utilized in a complex algorithm that was computer generated and gave a probability for the hospitalized patient being alive in 2 and 6 months' time.[25] While the mathematical model is complex and not suitable for routine use by the clinician at the bedside and the information provided (chance of being alive in 6 months) is relevant to only a small minority of cancer patients referred to hospice/palliative care, it shows that application of epidemiological methodology has the potential to provide the clinician with very accurate prognostic data.

Palliative Prognostic (PaP) score[24]

The Italian group who have identified elevated white cell count and low lymphocyte percentage as predictive of a poor survival have looked at combining these laboratory values with other parameters to develop a simple model for predicting survival that is useful for the palliative care/hospice clinician. As a result of multivariate analysis of more than 30 parameters, performance status, symptoms, and the haematological parameters are included with the CES in the final mathematical model. Points are allocated for each of these factors, and these subscores are then summed to give a final score, known as the Palliative Prognostic (PaP) score which predicts for short-term survival, as shown in Table 6.

In developing the PaP score system, the investigators found that this model is highly predictive of short-term survival and is able to split a heterogeneous sample of patients with far-advanced cancer (median survival around 30 days) into three groups, that is, those with a high (>70 per cent), intermediate (30–70 per cent), and low (<30 per cent) chance of still being alive in 30 days. The range of PaP scores, readily calculable at the bedside at the time of first contact with the patient, is 0–17.5, higher scores representing worse survival. Cut points of 5.5 and 11 for the three groups (i.e. 0–5.5 for the high-probability group, 6–11 for the intermediate, and 11.5–17.5 for the low-probability group) have been identified.

The PaP score has been subsequently validated by the investigators in almost 500 Italian patients, the overwhelming majority of whom were being visited by community care teams,[60] and independently in 100 hospitalized terminally ill patients in Australia.[83] The PaP score continues to be developed and a new version incorporating cognitive failure has been proposed by the investigators.

Table 6 How to compute PaP score[24]

	Partial score
Dyspnoea	
No	0
Yes	1
Anorexia	
No	0
Yes	1.5
Karnofsky performance status	
≤30	0
10–20	2.5
Clinician's estimate of survival (weeks)	
≥12	0
11–12	2
7–10	2.5
5–6	4.5
3–4	6
1–2	8.5
Total white cell count	
≤8.5	0
8.6–11.0	0.5
≥11	1.5
Lymphocyte percentage	
20–40	0
12–19.9	1
<12	2.5
Risk groups	*Total score*
A (30 day survival probability >70%)	0–5.5
B (30 day survival probability 30–70%)	5.6–11
C (30 day survival probability <30%)	11.5–17.5

Simple Indicator (Japan)[56]

Performance status and symptoms are combined to form a Simple Indicator to predict short-term survival in terminally ill cancer patients.[56] The Simple Indicator dichotomizes heterogeneous groups of patients according to whether or not they will live for more than 3 weeks or more than 6 weeks. The indicator performed well in the hands of its originators, having a high level of accuracy for both time points (84 and 76 per cent, respectively). It is unclear how the authors actually use the indicator to distinguish between the two groups: the indicators in both groups are a PaP Scale (see section on performance status) score of 10–20, dyspnoea at rest and delirium, with oedema being an additional risk factor for 6-week survival but not for 3-week survival.

GBU Index[84]

Over the past 10 years, the North Central Cancer Treatment Group of the United States has also identified performance status and nutritional factors as being predictive of short-term survival in patients enrolled in chemotherapy trials. Recently, this group has reported the 'GBU' (i.e. good, bad, or uncertain) Index which, like the Australian model and the Simple Indicator, uses combinations of four factors to stratify patients into three prognostic groups (good, bad, or uncertain chance of surviving 1 year). The GBU Index is most useful in patients with performance status scores ECOG 0–1. Like the Manchester Index, GBU has little relevance to the palliative care population, but it helps to further this interesting concept.

Formulating a prognosis in diseases other than cancer

Even more so than cancer, prognosis is critical to the discussion of terminal care in patients with various eventually fatal illnesses such as CHF, COPD, and Alzheimer's disease.[85–88] In the United States, such patients must have a prognosis of less than 6 months 'if the disease follows its usual course' to meet referral criteria to hospice programmes. In other countries, accurate prognostic information is important for the many other reasons identified in the introduction section.

However, formulating a prognosis in these illnesses may be more complicated than it is in cancer because of the difference in the death trajectories. Many of these illnesses may have precipitous declines that may not be reversible due to acute exacerbations [Fig. 1(c)]. As a result, the risk of dying can fluctuate wildly, soaring during acute exacerbations of illness and receding if the process can be stabilized.[89] For example, ER physicians identified 17 per cent of patients admitted for acute exacerbations of heart failure as having less than 10 per cent chance of surviving 90 days, when in fact 67 per cent did not survive.[90] The CES for hypothetical COPD patients with respiratory failure revealed marked variability in estimates.[91]

Nevertheless, there are some similarities with advanced cancer in terms of how one formulates a prognosis in the patient who is terminally ill with a non-cancer diagnosis. Firstly, the 'McKillop' model of prognostication

(Fig. 3) presumably remains relevant: pathology, clinical features, and environmental factors all contribute to the one general and individual prognoses as they do in cancer.[21] Secondly, performance status seems to be a useful global measure of survival in both types of conditions. Thirdly, the emotional and mental status of the patient and family influence the length of survival. Fourthly, the rate of disease progression is important in both the rate of hospitalization and the rate of development of new complications, especially in non-cancer diagnoses.

There are general and specific indicators of the terminal stage of non-cancer diagnoses.[85,92,93] The general ones are impaired performance status and impaired nutritional status. As for cancer, impaired performance status plays an important role in prognostication; it has been shown to predict mortality in the elderly in several studies,[94] and is the basis for the current (United States) National Hospice Organization (NHO) guidelines on prognostication in non-cancer illnesses.[95] Nutritional status is also significant: patients who experience a greater than 10 per cent weight loss over 6 months have been shown to have an increased risk of dying. Decreased serum albumin is also associated with mortality, especially if it is less than 25 g/dl.[96] When impaired performance status and impaired nutritional status occur together, they are highly predictive of short-term mortality.

Unfortunately, in the SUPPORT study, predictions of having less than 6-month survival in the subset of patients with CHF, COPD, and chronic liver disease (CLD) but without malignancy, multi-organ system failure, or acute respiratory failure were very inaccurate.[97] Not only were 70 per cent of individuals who were identified as being expected to die in 6 months still alive at the end of that period, but 54 per cent of those not expected to die in the period did so. Most strikingly, 41 per cent of patients given less than 10 per cent chance of surviving 6 months survived beyond this time frame. Even in the last 2–3 days of life, patients with CHF and COPD were given an 80 and 50 per cent chance of surviving 6 months, respectively.

With regard to individual disease indicators, the following specific predictors have been identified.

- *CHF:* age greater than 64 years, New York Heart Association (NYHA) Class, left ventricular ejection fraction less than 20 per cent, dilated cardiomyopathy, uncontrolled arrhythmias, systolic hypotension, and chest X-ray signs of left heart failure are all associated with poor short-term survival. The NHO criteria for a prognosis of less than 6 months are: (i) NYHA Class IV (chest pain and/or breathless at rest/minimal exertion) and (ii) already optimally treated with diuretics and vasodilators.
- *COPD:* advanced age, forced expiratory volume at 1 s (FEV_1) of less than 30 per cent, and pulmonary hypertension with cor pulmonale/right heart failure are poor prognostic signs. The NHO criteria include: (i) dyspnoeic at rest, (ii) on 24-h home oxygen with pO_2 less than 50 mm Hg and/or pCO_2 more than 55 mm Hg, and (iii) documented evidence of cor pulmonale.
- *Alzheimer's disease:* functional status appears to be the main predictor of survival. The onset of inability to walk unaided indicates entering the final phase of the illness. In one study, 30 per cent patients with dementia who were greater than 90 years of age and referred to a United States hospice programme were alive 3 years later.[98] NHO criteria include: (i) advanced disease (unable to walk independently and/or hold a meaningful conversation) and (ii) onset of medical complications (e.g. aspiration pneumonia, UTI, decubitus ulcers).
- *NHO criteria* are also available for HIV/AIDS, CLD, renal failure, stroke, coma, and motor neurone disease.

Few prognostic models have been developed for predicting survival in terminal non-cancer illnesses. The HELP study developed a nomogram for accurately estimating the length of life in the hospitalized elderly (>80 years of age) using a limited amount of clinical information, but has not been widely validated.[25] Gender, duration of illness, age at onset, Mini-Mental State Examination score, and extrapyramidal or psychotic features have been combined in a validated model that predict time to nursing home placement or death for patients with Alzheimer's disease.[99]

Communicating a prognosis

While foreseeing is the formulation of a prognosis by a clinician, foretelling is the specialized form of doctor–patient communication of a prognosis. The issue here is not merely whether and how physicians formulate prognosis, but also whether and how they might communicate them. Predicting survival in patients with far-advanced cancer and communicating the prognosis can be seen to have much in common with other forms of 'breaking bad news' in patients with a life-threatening illness.

Why communicate the formulated prognosis to the patient?

In the last 30 years, there has been a sea change in attitudes regarding disclosure of information to patients with cancer. It is now expected that the oncologist would have an open and frank discussion with the patient at the time of initial diagnosis about all aspects of the disease, including what the future holds, especially in terms of what can be expected from treatment.

Despite this openness, it is unclear what patients want in terms of prognostic information. Physicians in turn often regard it as taboo to talk about the length of time remaining for a patient perceived to be in the terminal stage of their illness. The reasons for this are multifactorial. Firstly, we still live in a death-denying society. Secondly, doctors' prognoses are notoriously inaccurate and many doctors are not confident about their prognosis-formulating skills—the popular culture is full of stories of patients 'beating the odds'.[100] Thirdly, it is dramatic and unpleasant for the doctor to forecast that the patient's death is imminent—not only does the doctor have to admit that medicine as an institution and they as an individual physician have 'failed', but they also will be apprehensive about how the patient will react to the prognosis and how they will react if the patient becomes very emotional. Furthermore, physicians are poorly prepared for the tasks of formulating and communicating prognosis, with medical schools, textbooks, and journals all tending to neglect prognostication.[19]

Physicians cope with the stress of having to formulate or communicate prognoses by adopting certain 'norms' of behaviour regarding prognostication (Table 7):

Foretelling an accurate prognosis is important because there is data that patients who are optimistic about their outlook will demand more aggressive life-sustaining treatment than those who are pessimistic about their outlook. If this optimism is unrealistic, this could have bad consequences for the patient if the aggressive life-sustaining treatment that they demand is futile and overly-burdensome for them. Moreover, most studies show that most patients want and need prognostic information in order to make the best possible clinical and personal decisions.[101] If this optimism is discordant with what the physician foresees as the prognosis, then there are a number of possible explanations for the discrepancy:

- the doctor has not given the patient a diagnosis/prognosis;
- the doctor has, but the patient is in denial;
- the doctor has, but the patient has misinterpreted what the doctor has said; and

Table 7 Norms of prognostication[19]

Do not make predictions
Keep what predictions you make to yourself
Do not communicate predictions to patients unless asked
Do not be specific
Do not be extreme
Be optimistic

- the doctor has said something vague or more optimistic than what he believes.

One study sought to shed light on these possibilities.[102] It involved asking physicians to formulate prognoses in specific patients of theirs and then asking them to state what they would communicate to these patients if the patients insisted on being told their prognosis. As mentioned previously, the formulated prognosis (median 75 days) was overly optimistic by a factor of 3 (median actual survival 26 days) (Table 8). They found that the doctors would give a frank disclosure of their prognosis to 37 per cent, not offer any prognosis to 23 per cent of patients, and offer a discrepant prognosis in 40 per cent, with the majority (70 per cent) of the discrepant prognoses in the over-optimistic direction. The authors' conclusion is that many patients are thus 'twice removed' from the reality of their outlook, because not only is the prognosis not formulated accurately but also the prognosis is then often communicated even more optimistically, a point illustrated by Fig. 4. This may help to explain the discrepancy between doctors and patient's perspective on their illness. The authors also examined various patient, prognostic, and physician characteristics to see if they correlated with the different categories of disclosure type.

Why might the physician want to disclose a prognosis that is more optimistic than what they believe it to be? Other work has identified the phenomenon of the 'self-fulfilling prophecy' in the psychology of the physician, and the possibility that giving an overly-optimistic prognosis to the patient will produce a better outcome than would have otherwise happened—and vice versa for a pessimistic prognosis. There is other data to support the view that doctors believe in the self-fulfilling prophecy and that being hopeful/optimistic produces better outcomes.[103] Because of the clear importance of maintaining hope in oncology, the task of foretelling an accurate prognosis to a patient with terminal cancer may be a greater challenge than accurately foreseeing it.

The first three norms listed above relate to the 'when' of prognosticating. Most patients with an eventually fatal illness are interested in some discussion about their preferences for end of life care and a meaningful discussion can only take place if the patient has a realistic understanding of where they are situated in the trajectory of their illness. It is well documented that there is a discrepancy between what physicians and patients understand about the goals of treatment and what the future holds throughout the spectrum of the cancer illness, and this has been documented in the terminal phase as well.

Table 8 Physicians' overestimates of patient survival, by observed and predicted survival[2]

Duration of survival (days)	% overestimate in survival (mean)	*N*
Observed		
1–30	795	251
31–90	288	130
91–180	136	49
>180	71	38
Overall	526	468
Predicted		
1–30	192	150
31–90	382	144
91–180	501	119
>180	1872	55
Overall	526	468

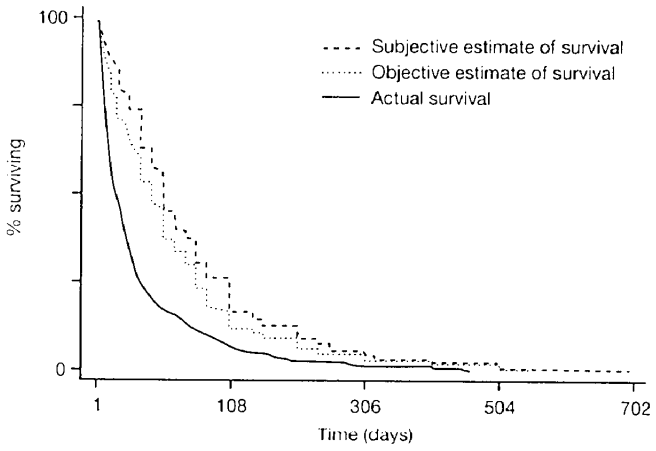

Fig. 4 Relationship between subjective, objective, and actual survival.[102] The graph illustrates the differences between actual survival, formulated 'objective' survival (told to the investigators), and communicated 'subjective' survival (that would be told to patients) in 300 terminally ill cancer patients. The median actual survival was 24 days, the median objective prognosis was 75 days, and the median survival disclosed to the patient was 90 days. *Source:* Lamont and Christakis, 2001.

How to communicate the formulated prognosis to the patient

While we have clarified what prognostic information the physician should try to provide in terms of significant content and scientific authority, the best process for conveying the prognosis remains problematic. In fact, it has been called the 'next communication frontier for oncology'.[104] There seem to be a number of preconditions to be fulfilled. Firstly, the doctor has to be willing to disclose the prognosis truthfully, and as we have already stated, the norms of medical practice counteract this. Secondly, a single conversation may not be sufficient: an open, supportive, and ongoing dialogue may often be required. Thirdly, development of communication aids such as question prompt sheets for patients/families or tools for illustrating concepts like probabilities that are difficult to simply explain need to be explored.

Communicating the prognosis—especially when it is unfavourable—is best seen as the prototype of breaking bad news. Thus, the doctor needs to be truthful, accurate, empathetic, and still try to foster hope. The rules for breaking bad news in other contexts should be followed: the doctor begins by ensuring the setting is as optimal as possible (i.e. privacy, sitting, partner), then ascertain how much information the patient wants, then ascertain what they already know, then deliver the news accordingly. The doctor should check that the patient has understood, then arrange to return subsequently to check that it has been understood, answer any more questions, and ensure the patient is coping.

Conclusion

Prognostication remains a controversial topic in palliative care. In the past 20 years, much research has been undertaken to identify ways of improving the accuracy and precision of clinicians' estimates. While we are now in a better position to give the patient '*x* per cent chance of surviving for *y* weeks/months', predictions that are precise enough to drive treatment plans remain elusive. Furthermore, models that predict survival should be thought of like any diagnostic test, that is, they should not be interpreted in isolation but as a way of improving the pre-test probability of survival, which is based on clinical judgement.

Clinical judgement alone may be sufficient if the issue is acknowledging that there is a probability of dying from an illness in the foreseeable future. The SUPPORT study showed that patients will change their planning behaviour once they understand that the chance of surviving beyond 6 months is small.

What ultimately may be needed is not so much an accurate prediction of time but an acknowledgement of the possibility of dying, communicated carefully by the compassionate and skillful physician.

Summary

- Prognostication is important in end of life care.
- The precision of the survival estimate depends on the reason for prognosticating.
- Doctors (and other health care professionals) are not very accurate when making temporal estimates in individual patients, although this may be improving.
- Experience improves prognostication accuracy, but this is modified by the closeness of the doctor–patient relationship.
- Probabilistic predictions are more accurate.
- The clinical estimate of survival is a powerful independent prognostic indicator.
- In general, patients with a poor performance status live for shorter periods than those who are more functional.
- Symptoms like anorexia, breathlessness, and confusion are important predictors that an individual is rapidly approaching the end of life.
- QOL scores may be more powerful than KPS scores or symptom reports in predicting survival.
- Simple, reliable, and valid prognostic models that combine these factors have been developed and can be readily used at the bedside of terminally ill cancer patients.
- Predicating survival in patients dying of diseases other than cancer is much harder.
- Communicating survival predictions is an important part of cancer care.

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The interdisciplinary team

J. Norelle Lickiss, Kristen S. Turner, and M. Lois Pollock

Introduction

A team is a strategy to achieve a goal, a means to an end. Team efforts centred on facilitating human flourishing in the face of eventually fatal illness, and especially in the face of approaching death, need clearly articulated goals, reformulated as often as necessary, in the light of changing circumstances and ethical dimensions. The increasing complexity of the tasks involved in palliative care as demonstrated in this book, and in the practice of palliative medicine as an ingredient of care, calls for a recognition of the increasing complexity (and multiplicity) of teams involved in the care of even one patient and his/her significant others.

The following scenarios may indicate the variability of the tasks and the challenges for interdisciplinary teams called to supplement the efforts of the core of any team: the patient and his or her closest associates. The questions may be asked of every case: What needs are obvious? At what points in the story? And what teams were involved in this patient's care?

1. A young village woman with locally advanced cancer of cervix, is brought by her husband to a city hospital in a developing country. She has severe pain in the left side of her pelvis, extending down the left thigh and into her calf. She can neither walk without pain nor sleep. The gynaecologist and the clinic provided her with paracetamol tablets. The hospital permits three injections of morphine in the post-operative period, but no morphine is permitted for medical use in other circumstances. There is no oral morphine. There are small supplies of codeine. Radiotherapy is available, with a 2-month waiting list: the cost of radiotherapy is equivalent to one quarter of her family's annual income. The woman has three small children in the village. There is a nurse at the village aid post, and arrangements are made for this patient to be taken home for care until radiotherapy can be commenced.

2. A village-based man, aged 40, father of five children, is found in a base hospital in a developing country to have advanced hepatocellular cancer. The family is advised to take him home to care for him until he dies, with the help of a nurse at a village aid post.

3. A professional man, 45, had melanoma excised from his upper back, in a major surgical referral centre in a university hospital. Two years later, he had a lump in the axilla (proven recurrence) excised and had local radiotherapy. Within 3 months, whilst remaining well and active he developed pain in the sacral region, worse on walking and he went to his local hospital. A fracture was noted on fifth lumbar vertebra, and he was transferred to the university hospital. Within the next few days pain had began to radiate down the anterior and lateral thigh, and although neurological tests were normal, he noted slight loss of power in right leg especially hip flexion and constipation for several days. A palliative medicine consultant recommended change in the analgesic regime and MRI, which demonstrated a mass near the cauda equina. Radiotherapy was begun that evening. The patient was emotionally shattered by the unequivocal evidence of metastatic melanoma. He does not wish his wife to be told that he has incurable and eventually fatal melanoma. A trial of chemotherapy (investigative) will be undertaken.

4. A woman in her 80s was sent down from a rural area, for surgery in a city hospital for presumed disc protrusion. Adenocarcinoma was found at the site: there was no obvious primary cancer. She became septic in the post-operative period, with delirium. A decision was made (with involvement of her daughter) for comfort care, with if possible,