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Prognostication of Survival in Patients With Advanced Cancer: Predicting the Unpredictable?

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Abstract

Background—Prognosis is a key driver of clinical decision-making. However, available prognostication tools have limited accuracy and variable levels of validation.

Methods—Principles of survival prediction and literature on clinician prediction of survival, prognostic factors, and prognostic models were reviewed, with a focus on patients with advanced cancer and a survival rate of a few months or less.

Results—The 4 principles of survival prediction are (a) prognostication is a process instead of an event, (b) prognostic factors may evolve over the course of the disease, (c) prognostic accuracy for a given prognostic factor/tool varies by the definition of accuracy, the patient population, and the time frame of prediction, and (d) the exact timing of death cannot be predicted with certainty. Clinician prediction of survival rate is the most commonly used approach to formulate prognosis. However, clinicians often overestimate survival rates with the temporal question. Other clinician prediction of survival approaches, such as surprise and probabilistic questions, have higher rates of accuracy. Established prognostic factors in the advanced cancer setting include decreased performance status, delirium, dysphagia, cancer anorexia–cachexia, dyspnea, inflammation, and malnutrition. Novel prognostic factors, such as phase angle, may improve rates of accuracy. Many prognostic models are available, including the Palliative Prognostic Score, the Palliative Prognostic Index, and the Glasgow Prognostic Score.

Conclusions—Despite the uncertainty in survival prediction, existing prognostic tools can facilitate clinical decision-making by providing approximated time frames (months, weeks, or days). Future research should focus on clarifying and comparing the rates of accuracy for existing prognostic tools, identifying and validating novel prognostic factors, and linking prognostication to decision-making.

Keywords

communication; death; decision-making; prognostic tools; palliative care; prognosis; survival

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Introduction

In the last months, weeks, and days of life, patients with advanced cancer may face numerous decisions regarding their personal affairs and health care, many of which depend on how long they will live. For example, patients were less likely to choose chemotherapy at the end of life if they understood that they had a short survival rate.[1,2] Similarly for health care professionals, prognosis is a key determinant of clinical decision-making because the risk:benefit ratio for many interventions increases as patients approach the last weeks of life. Chemotherapy given to a patient with months of life expectancy may result in tumor response, symptom control, and improved survival; however, the same chemotherapy regimen could cause life-threatening complications if administered to a patient with a poor performance status and a short survival rate.[3,4] Moreover, palliative resection, total parenteral nutrition, and insertion of an indwelling pleural catheter are generally appropriate for patients with at least a few months of life expectancy.[5] Moreover, hospice eligibility is based on a survival of 6 months or less. One study showed that patients were more likely to be referred earlier to hospice if their health care professionals made an accurate prediction of survival.[6]

Prognosis-based decision-making depends on an ability to accurately estimate survival, which has been a challenge for health care professionals and researchers alike.[7] The process of prognostication can be divided into formulation (foreseeing) and communication (foretelling).[8,9] Clinicians may formulate prognosis either subjectively (ie, clinician prediction of survival based on intuition) or objectively (ie, actuarial prediction of survival based on prognostic factors and models). Despite the availability of validated prognostic factors and tools, most health care professionals rely on clinician prediction of survival to estimate prognosis because clinician prediction of survival is instantaneous, convenient, and easy to understand. Although clinician prediction of survival often incorporates many known prognostic factors in its determination, each may be assigned a variable weight by different health care professionals. Coupled with variable knowledge, clinical experience, and personality, this results in heterogeneous and often optimistic estimations of life expectancy.[10,11]

Progress has taken place in the science of prognostication. In this article, some important principles of survival prediction are discussed and the medical literature on clinician prediction of survival, prognostic factors, and prognostic models are reviewed, focusing on patients with advanced cancer with a survival rate of months or less. The future research directions are also be explored.

Principles of Prognostication

Prognostication is a process instead of an event. A patient’s prognosis may change based on treatment response, development of acute oncological complications (eg, hypercalcemia, spinal cord compression, pulmonary embolism), or competing comorbidities (eg, heart failure). In a study of 352 patients admitted to acute palliative care units who had a median survival of 10 days, the presence of acute symptomatic complications, such as pneumonia, peritonitis, metabolic acidosis, and gastrointestinal bleed, was associated with a higher risk

of mortality.[12] Patients with a larger number of acute complications also had a shorter survival.[12] Thus, it is important for health care professionals to revisit prognosis with patients over time. Sentinel events such as cancer diagnosis, disease progression, and hospitalizations should trigger a prognostic discussion.

Prognostic factors may vary by the stage of disease. In patients with early stage cancer, prognosis may be driven by cancer biology such as tumor stage, histological grade, and mutation status (Table 1). By contrast, prognostic variables in patients with far advanced disease typically consist of patient-related factors such as performance status, dyspnea, delirium, and cancer anorexia/cachexia.[13] In the last days of life, distinctive, bedside physical signs may signal that death is imminent.[14,15] Thus, it is important to understand the inception cohort for which the prognostic factors/models were derived and apply the study findings to the appropriate patient population. Terms used to describe the inception cohort in the literature, such as end of life and terminally ill, have been heterogeneously defined.[16] A systematic review of the literature clarified that both of these terms refer to patients with "months or less of life expectancy," which represent the target population of this review.[17]

Accuracy is an elusive concept in prognostication research. This is because not all prognostic studies consistently report accuracy; and, when reported, different investigators may use different metrics to assess accuracy, the accuracy of a prognostic tool varies by patient population and the time frame of prediction, and very few studies examining novel prognostic factors have incorporated a comprehensive list of known prognostic variables for benchmarking and examined reclassification. Discrimination and calibration are 2 key aspects of accuracy.[18-20] Discrimination reflects how well a prognostic tool differentiates between patients who died and remained alive by a specific time frame. The Concordance statistic (C-statistic) is often used to examine discrimination, with a value between 0.5 and 1. For a C-statistic to be significant, the 95% confidence interval should not cross 0.5. Because the C-statistic is less sensitive to the addition to a novel prognostic marker to an existing model, reclassification statistics, such as the reclassification calibration statistic, net reclassification improvement, and integrated discrimination improvement should be used to assess the degree of improvement with addition of the new factor.[21,22] Calibration represents how well the predicted probability of survival based on a prognostic model matches the actual outcomes. A model is considered to have satisfactory calibration (or goodness-of-fit) if the Hosmer–Lemeshow test gives a *P* value greater than .05.[23,24] Furthermore, the prognostic accuracy could be estimated with sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy. To advance the science of prognostication, the accuracy of existing and novel prognostic markers and models need to be routinely assessed.

It may not be possible to prognosticate with 100% accuracy (ie, 100% sensitive and 100% specific). Because death is a probabilistic event, its exact timing cannot be predicted with certainty.[25] With disease progression, the likelihood of acute catastrophic complication increases, such as myocardial infarction, pneumonia, and massive bleeding.[12] Some patients may survive longer than expected, whereas some may die earlier than expected.[26] Thus, health care professionals may want to avoid providing specific numbers when discussing prognosis, because doing so could be misleading.[27] Instead, they can acknowledge the

uncertainty, guide decision-making by providing general time frames (eg, weeks to months), and advise patients and families to expect the unexpected.

If we can make decisions based on approximations, why should we still strive to improve the accuracy of survival prediction? It is because a higher accuracy can offer health care professionals greater confidence when communicating with patients and families while also bringing greater clarity to decision-making.

Clinician Prediction of Survival

Over the last decades, clinician prediction of survival has evolved from the classic, temporal question, "How long do I have?" to the surprise and probabilistic questions. Table 2 highlights the question format and advantages and disadvantages for each approach. The results of some studies also suggest that how the question about prognosis is asked may impact its rate of accuracy.[10,29,32]

Temporal Question

With the temporal approach, the health care professional is asked the question, "How long will this patient live?" The answer may be provided as a specific time frame (eg, 3 days, 6 months). This is the most commonly used approach to estimate the rate of survival. The answer is relative easy to formulate, communicate, and understand. However, it is often not specified if the answer represents the average, median, maximal, or minimal expected survival, possibly resulting in confusion among health care professionals and patients. Furthermore, some health care professionals may find it psychologically challenging to provide a number and communicate with patients an "expiration date."

Temporal clinician prediction of survival often results in systematically overestimation and has a 20% to 30% rate of accuracy, defined as a predicted survival rate of within ± 33% of actual survival.[10,11] Christakis et al[28] asked 343 physicians to estimate the survival for 468 patients at the time of hospice referral; the median survival in this cohort was 24 days. A total of 20% of predictions were accurate, 63% were overly optimistic, and 17% were overly pessimistic.[28] Female patients, certain medical subspecialties, lack of clinical experience, and a longer duration of the doctor–patient relationship were associated with less accurate predictions.[28] Another study that included advanced patients with cancer with a median survival of 12 days found that younger patient age was associated with less accurate, temporal clinician prediction of survival.[10]

Surprise Question

The surprise question poses the following to the health care professional: "Would I be surprised if this patient died in (specific time frame)?" The health care professional can answer no if he or she would not be surprised that the patient would die within the predefined period of time and yes" if he or she felt otherwise. Rather than a number with infinite possibility, as in the temporal question, the answer is binominal (yes or no), which may help to reduce the likelihood of error. However, each health care professional may have a different threshold for "surprise."

Moss et al[29] asked 4 oncologists to estimate the 1-year survival rate of 853 patients with cancer using this surprise question. The positive predictive value was 41%, the negative predictive value was 97%, and the accuracy rate was 88%.[29] In other words, the surprise question was helpful in identifying patients who would live beyond 1 year but less able to identify patients who were going to die within that time frame. In another study, 42 general practitioners in Italy answered the surprise question for 1-year survival in 231 patients with advanced cancer.[30] The positive predictive value was 84%, negative predictive value was 69% and accuracy was 76%.[30] Most recently, Hamano et al. examined the prognostic accuracy of the surprise question in 2361 Japanese patients who had a median survival of 33 days. With the "7-day" surprise question, the sensitivity was 85%, specificity was 68%, positive predictive value was 30%, negative predictive value was 96%, and accuracy was 70%. In contrast, the "30-day" surprise question had sensitivity of 96%, specificity of 37%, positive predictive value of 58%, negative predictive value of 90%, and accuracy of 65%.

The surprise question has been used to identify patients who have a limited survival and, thus, may benefit from various services such as palliative care referral and advance care planning discussions; however, the usefulness of this approach needs to be further validated. One qualitative study examining the use of the surprise question among general practitioners identified some potential concerns, including its subjective nature, difficulty in defining a precise time or event when the health care professional would switch the answer from "yes" to "no," and disagreement that a "no" answer represents the ideal time for specific actions such as advance care planning discussions.[31]

Probabilistic Question

The third approach to clinician prediction of survival employs the probabilistic question. Instead of the "surprise" wording, it asks the health care professional to state the probability of survival within a specific time frame (at 10% increments from 0% to 100%). The response is considered accurate if the health care professional provided a probability of at least 70% and the patient was alive by the prespecified time frame, or if health care professional provided a probability of up to 30% and death occurred within the time frame. By definition, any probability between 40% and 60% is considered as inaccurate because the health care professional expressed ambivalence. The probabilistic approach has a potential advantage over the surprise question because it is not dependent on how "surprise" is interpreted.

The probabilistic approach was tested in a cohort of 151 patients with advanced cancer admitted to an acute palliative care unit.[10] The median survival was 12 days.[10] Both physicians and nurses were asked to provide their estimation of survival from the time of admission related to the following time frames: 24 hours, 48 hours, 1 week, 2 weeks, 1 month, 3 months, and 6 months, and the respective accuracy rates were 71%, 66%, 58%, 56%, 67%, 86%, and 96% for physicians and 91%, 86%, 61%, 53%, 60%, 79%, and 88% for nurses.[10] By contrast, the rate of accuracy was significantly lower with the temporal approach (32% for physicians and 18% for nurses).[10] Because the same group of health care professionals made predictions in the same cohort of patients, the findings from this study suggested how we pose the question may yield answers with different accuracies.[10]

In another study, physicians and nurses provided daily prognostication in 311 patients from the time of admission to an acute palliative care unit until death or discharge using both the probabilistic approach (24- and 48-hour time frames) and the temporal approach.[32] The rate of accuracy of the probabilistic approach (40% to 100%) was consistently higher than the temporal approach (10% to 30%) among both professions, although its rate of accuracy decreased as death approached.[32] Nurses were more accurate than physicians with the probabilistic approach but not with the temporal approach, suggesting that the time of prognostication, the type of health care professional, and the method of clinician prediction of survival are all determinants of the rate of accuracy.[32] Finally, the result highlights the difficulty in identifying patients who are imminently dying even among experienced palliative care physicians and nurses.[26,32]

Actuarial Estimation of Survival

Prognostic factors can generally be classified as disease- and patient-related factors. Patient-related factors have a prominent role in prognostication in the last months or weeks of life. Many tumor-related markers, such as circulating tumor cells, have been shown to have prognostic and predictive utility in patients with metastatic disease; however, their role in patients with only months or weeks of survival need to be further examined.[33] For the purpose of this review, the discussion is focused on the most validated prognostic factors and models as well as on several novel prognostic factors.

Prognostic Factors

Among the multiple symptoms with prognostic significance in the advanced cancer setting are the 4 Ds: decreased performance status, dysphagia and cancer anorexia–cachexia syndrome, delirium, and dyspnea.[13,34] Performance status declines in the months before death, with a steeper deterioration in the weeks and days preceding death.[35,36] Patients with a lower performance status had a higher likelihood of developing serious adverse events when receiving systematic therapy.[3,4] In a study involving 1,655 patients with advanced cancer, Eastern Cooperative Oncology Group performance scale, Palliative Performance Scale (PPS), and Karnofsky Performance Scale were strongly associated with survival, with C-statistics of 0.64, 0.63, and 0.63, respectively.[37] A web-based program (Prognostat) is available that provides the historical rates of survival based on PPS, age, sex, and cancer diagnosis; however, further validation is required.[38]

Cancer anorexia–cachexia is another prognostic factor seen in patients with advanced cancer and is associated with elevated inflammatory response and poor nutritional status; loss of appetite is a poor prognostic marker.[39] Malnutrition assessed by either subjective global assessment or other nutritional indices has also been found to be associated with shortened rates of survival.[40-42] A multicenter study showed that a lower baseline body mass index and higher percentage of weight loss were both associated with shorten rates of survival, thus forming the basis for a prognosis-based staging system for cancer anorexia–cachexia.[43] Moreover, decreased lean body mass, a hallmark of anorexia–cachexia, has prognostic significance independent of the palliative prognostic score.[44]

Delirium is another syndrome associated with a shortened rate of survival.[12,45] Although delirium is potentially reversible in some patients, many patients with cancer develop irreversible or terminal delirium in the last weeks or days of life.[15,46,47] Multiple studies have also confirmed the prognostic role of dyspnea; in particular, patients with dyspnea at rest have a shorter rate of survival than those with episodic dyspnea alone.[48,49]

Other objective, physiological measures also have prognostic utility. Phase angle, a marker of cellular membrane integrity and hydration, is lower in patients with shorter survival.[50,51] A prospective study of 222 patients with advanced cancer and a median survival rate of 106 days found that phase angle was a significant prognostic factor independent of Palliative Prognostic Score (PaP), hypoalbuminemia, and decreased lean body mass.[44] Hand-grip strength and maximal expiratory pressure that assess skeletal muscle and respiratory muscle functions, respectively, were also associated with survival in patients with advanced cancer.[51] These objective measures show some promise in survival prediction because they are reproducible, noninvasive, easy to use, portable, and inexpensive. However, they need to be further validated before they can be applied in routine practice.

Several laboratory abnormalities have prognostic significance in the advanced cancer setting. Markers of inflammatory response, such as elevated C-reactive protein, erythrocyte sedimentation rate, leukocytosis, lymphopenia, and neutrophil:lymphocyte ratio were associated with poor nutritional status and survival.[13,41,52] Other markers of decreased survival include hypoalbuminemia (indicative of malnutrition), hypogonadism (associated with decreased lean body mass and performance status), hypercalcemia (often related to tumor progression), hyponatremia, and elevated lactate dehydrogenase.[12,53-55] For example, patients with advanced solid tumors who presented with hypercalcemia have a median survival rate of 2 months.[56]

Prognostic Models

Multiple prognostic scoring systems have been developed for patients with advanced cancer. These prognostic models typically include many of the established prognostic factors discussed above. Table 3 illustrates several of the well-validated prognostic models in the advanced cancer setting, including PaP, the Palliative Prognostic Index (PPI), and the Glasgow Prognostic Score.[52,57-65,69,73-76,80-86] General time frames are provided by risk score categories for these 3 prognostic models. The original PaP score does not include delirium, although the addition of this variable to create the Delirium-PaP score results in slight improvement in its performance.[66] A modified version of the Glasgow Prognostic Score assigns no points (instead of 1 point) to hypoalbuminemia alone without an elevated level of C-reactive protein.[67] In all of these models, total score is calculated based on the number of prognostic factors (ie, higher score = worse survival) and a probability of survival by a defined time frame is provided based on the risk group category.

Other prognostic models have been derived from patients with only months or weeks of survival, including the Objective Prognostic Score, the B12/C-reactive protein Index, the Japan Palliative Oncology Study-Prognostic Index, the Chuang Prognostic Score, the Terminal Cancer Prognostic Score, and the Poor Prognosis Indicator.[68-76]

Despite the plethora of prognostic models, the one that is the most accurate or superior to clinician prediction of survival alone remains unclear. In a prospective study of 549 patients with advanced cancer and a median survival of 22 days, Maltoni et al[77] reported that PaP, Delirium-PaP, PPI, and PPS had respective C-indices of 0.72, 0.73, 0.62, and 0.63 and accuracy rates of 88%, 80%, 72%, and less than 50%. However, the PPI cutoffs used were different from earlier studies.[77] In a separate study, Stiel et al[78] examined the performance of PPI, PaP, and clinician prediction of survival in 84 patients with cancer. PPI had the highest correlation coefficient with actual rate of survival (0.68), followed by PaP (0.58) and clinician prediction of survival (0.56).[78] Clinician prediction of survival was examined as a categorical variable instead of as a continuous variable.[78] In a large prospective study in Japan, Baba et al. examined the feasibility and accuracy of PaP, Delirium PaP and PPI in 2361 patients in both hospital and home settings. Although PPI was completed more often, PaP and Delirium PaP scores had higher accuracy than PPI for 21 day survival prediction (C-statistic 0.79-0.89 vs. 0.75-0.84, $P<0.05$) and 42 day survival prediction (C-statistic 0.81-0.88 vs. 0.75-0.85, $P<0.05$).

The change in a prognostic score may also be useful for predicting survival, with the understanding that patients who deteriorate often have a worse prognostic score over time and vice versa. In a study of 2,392 patients with advanced cancer, Kao et al[79] found that the median PPI increased from 6 on day 1 to 7 on day 8 (P <.001). The median survival rate was 53 days with an improvement in PPI score, 36 days with a stable PPI score, and 22 days with PPI deterioration over the 1-week period.[79] The C-statistic for 30-day survival was 0.63 for a baseline PPI score, 0.64 for a PPI change score, and 0.71 for the combined baseline and change in PPI.[79] When only patients with a higher baseline PPI (ie, > 6) were included, the C-statistics for 30-, 60-, and 90-day survival rates were 0.66, 0.64, and 0.63 for the baseline PPI, respectively, and 0.72, 0.76, and 0.79 for the magnitude of PPI change between baseline and day 8.[80] The corresponding accuracy rates were 61%, 57%, and 55% for baseline PPI, and 71%, 79%, and 83% for PPI change, respectively.[80] By definition, the change score could only be used in patients who remained alive 1 week after the initial assessment, which may limit it utility to a certain extent.[80] Nevertheless, a change in PPI over only 1 week had prognostic value. Further studies are needed to examine the prognostic utility of change over different time periods and with different prognostic scores.

Future Directions

Accuracy Reporting

The discrimination and calibration of prognostic markers (eg, clinician prediction of survival, prognostic factors and models) should be consistently reported using standardized, predefined, and practical time frames (eg, 1 week, 1 month, 2 months, 3 months, 6 months) that would allow comparison across studies.

Clinician Prediction of Survival

How we pose the questions matters. In addition, the rate of accuracy of clinician prediction of survival varies by clinician factors, patient characteristics, and time frame of prediction. To date, the surprise question has only been tested with the 1-year, 30-day and 7-day

survival time frames in advanced patients with cancer. The probabilistic question has been examined with the time frames of 24 hours, 48 hours, 1 week, 2 weeks, 1 month, 3 months, and 6 months; however, this was only conducted in patients admitted to palliative care units. Thus, these rates of clinician prediction of survival must be further validated. A direct comparison of the accuracy rate of these approaches is also needed.

Prognostic Factors/Models

Existing—Validation of existing prognostic factors/models is important. Furthermore, comparison of the performance of these prognostic tools is warranted to help allow health care professionals to identify the most appropriate model(s) for clinical practice.

Novel—A better understanding of the physiological and pathological processes in patients with cancer may help develop novel prognostic markers. Research studies of novel prognostic markers should aim at improving the rate of accuracy of established prognostic model; thus, reclassification statistics should be consistently reported. The role of serial prognostication should also be further examined.

Diagnosis of Impending Death

Recognition that a patient has entered the last days of life presents a unique area for research. Instead of a prognostic question, this may be a diagnostic issue because the process of dying is irreversible. The results of some studies have suggested that several bedside clinical signs have very high specificity rates for impending death; however, further validation is required.[14,15]

Web-Based Programs

There are few web-based prognostication programs available for patients with advanced cancer. Web-based programs should be developed to facilitate the use of validated prognostic models for clinical decision-making. Existing programs (eg, Prognostat) currently have limited use.

Communicating Prognosis

Although it is beyond the scope of this review, how health care professionals discuss prognoses with patients and families also warrants further research. Should we give the maximum, minimum, and/or median survival times (as in the temporal approach), the probability of survival at various time points (as in the probabilistic question and prognostic models), or general time frames (ie, days, weeks or months)? Given that the rate of accuracy is below 80% for a vast majority of prognostic tools, perhaps communicating prognoses using general time frames would provide adequate information for decision-making while not being misleading. Ultimately, research studies are needed in this area.

Prognostic Factors

Clinical Decision-Making—More studies are needed to examine how prognostic tools can be used to guide clinical decisions, such as palliative care referral or chemotherapy discontinuation.

Clinical Trials: In addition to clinical decision-making, prognostic factors and models may be incorporated as eligibility criteria or stratification factors in clinical trials of oncology treatment. Currently, performance status is commonly included. Some prognostic markers may have both predictive and prognostic utility.

Conclusions

Clinician prediction of survival remains the most commonly used approach to formulating a prognosis, a fact that can be attributed to convenience (clinician prediction of survival already incorporates many existing prognostic factors), and few studies have demonstrated that use of prognostic models can significantly improve rates of accuracy. However, health care professionals often overestimate survival with the temporal question, and other clinician prediction of survival approaches, such as the surprise question and the probabilistic question, may estimate survival with a defined time frame and have moderate to high accuracies.

Prognostic factors in the advanced cancer setting include symptoms (eg, decreased performance status, delirium, dysphagia, cancer anorexia–cachexia, dyspnea), physiological changes (eg, decreased muscle function, lean body mass), and laboratory abnormalities (eg, increased C-reactive protein, hypoalbuminemia). Multiple prognostic models have been developed based on these prognostic factors, with the Palliative Prognostic Score, Palliative Prognostic Index, and Glasgow Prognostic Score being the most validated. However, the probabilities of survival generated by these models must be translated into an easy-to-understand format to facilitate clinical decision-making. Finally, research in novel objective prognostic markers such as phase angle may improve our rates of accuracy in prognostication.

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Table 1
Differences in Prognostic Factors Between Patients With Early and Advanced Cancer

	Early Stage	Advanced Stage
Prognosis	Years, decades	Months, weeks, days
Inception cohort	Cancer site specific Time of diagnosis Time of consultation	All cancer groups Admission/referral to palliative care or hospice
Prognostic factors	Clinical: stage, laboratory studies Pathological: histology, grade Molecular: gene, microarray Others: treatments, resources	Clinical: symptoms, laboratory studies Pathological: NA Molecular: NA Others: treatments, resources
Tools	Scores: IPI Programs: Adjuvant online	Scores: PaP, PPI Programs: PPS
Implications	Overall outlook on life span Worse prognosis = more intensive cancer treatment New cancer treatment → changes in prognostic factors	End-of-life planning Worse prognosis → limit cancer treatment Limited cancer treatment → same prognostic factors

IPI = International Prognostic Index, NA = not applicable, PaP = Palliative Prognostic Score, PPI = Palliative Prognostic Index, PPS = Palliative Performance Scale.

Table 2
Three Approaches to Clinician Prediction of Survival

Aspects	Temporal Question[10,32]	Surprise Question[29,30]	Probabilistic Question[10,32]
Question	How long will this patient live?	Would I be surprised if this patient died in (specific time frame)?	What is the probability of survival within a specific time frame
Answer	Specific time frame	Yes or no	0% to 100% (at 10% increments)
Definition of an accurate response	If estimated time frame was ± 33% of actual survival	If "no" answer and patient died within specified time frame or If "yes" answer patient remained alive by specified time frame	If answered ≤ 30% probability and patient died within specified time frame or If answered ≥ 70% probability and patient remained alive by specified time frame
Accuracy	20%–30%	76%–88% (1 year time frame)	53%–91% (6 months to 24-h time frames)
Advantage	Simple, quick Intuitive to provide Understand	Simple, quick Intuitive to understand	Simple, quick
Disadvantage	Subjective Unclear if time frame represents the average/median, maximal or minimal May be difficult emotionally to provide a specific number	Subjective Time frame dependent The threshold for "surprise" may vary by individual Yes/no answer only	Subjective Time frame dependent Probability needs to be interpreted

Table 3
Prognostic Models for Patients With Advanced Cancer

Models	Variables	Scoring	Survival Interpretation
Palliative Prognostic Score[57-60]	Clinician prediction of survival (0–8.5) Karnofsky performance scale ≥ 50% (2.5) Anorexia (1.5) Dyspnea (1) Leukocytosis (0–1.5) Lymphopenia (0–2.5)	Total score 0–17.5 points Higher score = worse survival	Risk group A (0–5.5 points): months of survival Risk group B (5.6–11 points): weeks of survival Risk group C (11.1–17.5 points): days of survival
Palliative Prognostic Index[80-86]	Palliative performance scale (0–4) Delirium (considered absent if caused by a single medication and potentially reversible) (4) Dyspnea at rest (3.5) Oral intake (0–2.5) Edema (1)	Total score 0–15 points Higher score = worse survival	Risk group A (0–4 points): months of survival Risk group B (4.1–6 points): weeks of survival Risk group C (6.1–15 points): days of survival
Glasgow Prognostic Score[52,61-65]	Albumin < 35 g/L (1) C-reactive protein > 10 mg/L (1)	Total score 0-2 Higher score = worse survival	Score = 0: months to years of survival Score = 1: months of survival Score = 2: weeks to months of survival