EPEC-O

Education in **P**alliative and **E**nd-of-life **C**are - **O**ncology

Participant's Handbook

Module 8

Clarifying Diagnosis and Prognosis

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Abstract

Accurate prediction and disclosure of diagnosis and prognosis is essential for both treatment and personal decision making. Physicians tend to be overly optimistic in their survival estimates and even more optimistic when they relay prognostic information to patients. This module reviews physician prognostication skills, the sources of prognostic information, and the role of integrated prognostic models and their limitations. It then presents a 6-step protocol to guide the communication and clarification of diagnosis and prognosis. Approaches for handling unrealistic expectations and denial are also discussed.

Key words

Prognosis, clinical prediction of survival (CPS), performance status (PS), Palliative Prognostic Index (PPI), formulated prognosis

Objectives

After studying this module, oncologists and other members of the cancer care team will be able to:

- Describe the difficulty inherent in prognostication.
- Contrast what is known with the limitations of current prognostic models.
- Apply the 6-step protocol to communicate and clarify diagnosis and prognosis.

Clinical case on trigger tape

A 75-year-old married corn farmer was referred by a surgeon to radiation oncology for treatment of hemoptysis secondary to stage IIIB non-small cell lung cancer. The patient reports a 6 month history of cough with occasional hemoptysis. It didn't seem that different from his smoker's cough. At his wife's insistence, he went to the doctor. A chest radiograph showed 'maybe a pneumonia' in the left lung and antibiotics were prescribed. Nothing changed. Repeat chest radiograph showed 'it wasn't better.' A CAT scan showed a mass with increased size of some of the lymph nodes. A bone scan was negative. He underwent mediastinoscopy which gave the diagnosis. He has continued to work and has his usual energy. His social history is remarkable for starting smoking when he was 14. He was married at 18 and kept smoking until about 5 years ago when his six kids and his wife finally convinced him to quit. He works on his family farm, although 3 of his sons help out a lot.

Introduction

It is customary for oncologists to convey information about prognosis. The vast majority of Americans want to know if they have a life-threatening illness and how long they have to live.[1,2] Studies in other cultures yield surprisingly similar data.[3,4] Although legitimate cultural variations are important, communicating diagnosis and prognosis in a direct and compassionate manner is likely to improve the patient's and family's ability to plan and cope, encourage realistic goals and autonomy, support the patient emotionally, strengthen the physician-patient relationship, foster collaboration among the patient, family, physicians, and other professionals, and be reassuring that the cancer care team will be honest, even when the news is not good.

Many patients ask about their prognosis. Others expect the oncologist will introduce the subject. Most want to have a sense of their future so they can plan their lives. Some are terrified and hope that you will reassure them that things are not so serious.

At times, understanding what a diagnosis and prognosis mean may be very confusing to patients and families and very challenging to oncologists. Patients and families do not always translate 'metastatic' disease to 'incurable' disease which is usually though not the full meaning of the situation. Furthermore, x% respond is not infrequently heard as 'x% are cured.'

As with communicating 'bad' news, family members may not want you to tell the patient her/his prognosis. Some fear the news will be so distressing that it will affect the patient adversely, even lead to her/his death.

Difficult for the oncology team

At times it may also be difficult for oncologists and members of the cancer care team who want to be on the 'hope' team to share the information when they don't want to believe the news either. To make this process easier, it may be helpful to reflect that information carefully shared is a gift to the patient and family who want it and minimizes the risk that patients will distrust the cancer care team.[2]

Determining prognosis

At diagnosis, recognized tumor-specific prognostic factors, eg, molecular markers, stage, grade, etc., modified by treatment- and patient-specific factors, eg, comorbid illness, performance status, disease signs and symptoms, provide general prognostic information.

Overestimation

Prognostication for advanced cancer, based on physician's clinical experience and intuition (formulated prognosis), is generally inaccurate. Physician estimates of prognosis for patients in palliative care programs tend to be overly optimistic by a factor of 3-5.[5,6]

In spite of this, physician estimates correlate with actual survival and are most accurate in patients with survival less than 6 months.[5,6,7,8]

In 7 out of 8 studies, physicians overestimated survival in patients with advanced disease.[7] Actual survival (AS) and clinical predictions of survival (CPS) from these trials are shown in Slide 6. The median CPS was 42 days, while the actual median survival was 29 days.

Table 1: Studies of clinical predictions of survival vs. actual survival

Study	# Patients	Median CPS (days)	Median AS (days)
Parkes et al[1]	71	28 (45-56)	21 (9-34)
Evans et al[2]	42	81 (28-182)	120 (43-180)
Heyse-Moore et al[3]	50	56 (33-84)	14 (7-28)
Maltoni et al[4]	100	42 (28-56)	32 (13-63)
Maltoni et al[5]	530	42 (28-70)	32 (13-62)
Oxenham et al[6]	21	21 (14-35)	15 (9-25)
Maltoni et al[7]	451	42 (21-70)	33 (14-62)
Christakis et al[8]	325	77 (28-133)	24 (12-58)
Overall	1,591	42 (28-84)	29 (13-62)

A meta-analysis of these studies suggests that survival is generally 30% shorter than predicted by CPS.[7] CPS was within one week of actual survival in 25% of cases and overestimated survival by 4 or more weeks in 27%.

In spite of the limited accuracy of physician estimates of prognosis, physician input adds accuracy and value to statistical models.[6,8,9] Sources of prognostic information include physician predictions, stage-specific survival data, performance status, signs and symptoms, and integrated models of prognosis.

Stage of cancer

Survival data for specific cancers by stage are widely available but not very useful to assess the prognosis of an individual patient. Natural history studies, though generally the experience of a single institution, provide insight into the variable course and prognosis of advanced cancer.

In a similar way, randomized trials which include a ‘best supportive care’ arm provide further natural history information—essential information to communicate to patients when relating the anticipated survival benefits from treatment for advanced disease.

For example, patients with untreated, advanced breast cancer have a median survival of more than 2 years, while those with untreated advanced head and neck cancer have a median survival of about 4 months.[10,11]

Performance status

Karnofsky

Performance status is a measure to quantify the functional status of cancer patients, and with the Karnofsky performance scale, to measure medical care requirements. Karnofsky performance scale, a reliable, valid, simple, and reproducible measure of patient function, is an independent predictor of survival.[12,13] The predictability of Karnofsky performance scale for survival is, however, valid only for patients with scores less than 50.[14,15] Data from the 1,592 patients in the National Hospice Study identified Karnofsky performance scale as the most important clinical factor estimating prognosis.[16] Karnofsky performance scale differentiated the survival time of 3 distinct patient groups: Karnofsky performance scale ≥ 50 (86.1 days), Karnofsky performance scale = 30-40 (49.8 days), and Karnofsky performance scale = 10-20 (16.8 days), see Table 1.

Table 1: Prognosis for patients on hospice based on Karnofsky performance status

Definitions	Rating	Criteria	Prognosis
Able to carry on normal activity and to work; no special care needed.	**100**	Normal no complaints; no evidence of disease. No special care needed.	
	90	Able to carry on normal activity; Minor signs or symptoms of disease.	
	80	Normal activity with efforts; some signs or symptoms of disease.	
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	**70**	Cares for self; unable to carry on normal activity or to do active work.	
	60	Requires occasional assistance, but is able to care for most of his personal need.	86.1 days
	50	Requires considerable assistance and frequent medical care.	
Unable to care for self; requires equivalent of institutional or hospital care; diseases may be progressing rapidly.	**40**	Disabled; requires special care and assistance.	49.8 days
	30	Severely disabled; hospital admission is indicated although death not imminent.	
	20	Very sick; hospital admission necessary; Active supportive treatment necessary.	16.8 days
	10	Moribund; fatal processes progressing rapidly.	
	0	Dead	

Loprinzi et al. have also demonstrated the ability of Karnofsky performance scale to define 3 advanced cancer patient populations with statistically distinct survival curves by univariate and multivariate analyses.[17] The strength of the association between performance status and survival appears to be time dependent; Karnofsky performance scale is of greater prognostic value when the anticipated survival is less than 3 months.[18]

ECOG/WHO

A simpler scale was developed by Zubrod and found to be as useful as the Karnofsky Score but more easily assessed by untrained observers.[19] The Eastern Cooperative Oncology Group (ECOG) and the World Health Organization (WHO) have adopted this scale.

In all studies, a score of 3 correlates with a prognosis of less than 3 months. A score of 4 correlates with a prognosis of less than 1 month.[20]

Table 2: Prognosis by ECOG/WHO performance status

Grade	Criteria	Median Prognosis
0	Fully active, able to carry on all pre-disease performance without restriction.	
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, eg, light house work, office work.	
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.	
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.	< 3 months
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.	< 1 month
5	Dead	–

Clinical signs and symptoms

Integrating the impact of various physical symptoms with performance status improves its predictive capability. A systematic review of prognostic factors in advanced cancer from 24 studies, examined more than 100 variables and identified cognitive factors, weight loss, dysphagia, xerostomia, anorexia, and dyspnea as independent survival factors for patients with advanced cancer.[18]

Palliative Prognostic Index

Prognostication is both art and science, and imperfect at best. Integration of data from multiple sources of prognostic information improves one's ability to predict outcome.[21, 22] The Palliative Prognostic Index (PPI) is a validated model to predict prognosis for advanced cancer patients.[23, 24] This model incorporates performance status, CPS, and specific clinical symptoms and signs. The model is able to predict 3- and 6-week survival in a cohort of advanced cancer patients with a sensitivity and specificity of 83% and 85% at 3 weeks and 79% and 77% at 6 weeks, respectively.[23]

Integration of signs and symptoms into a prognostic model for patients continuing on treatment is not available, and the PPI has not been evaluated in patients earlier in their disease course.

Advanced or metastatic solid tumors receiving antineoplastic therapy

A review of the median survival for patients with advanced or metastatic solid tumors reported in published phase III treatment trials during the last 5 years provides a broad view of the prognosis for patients receiving treatment for advanced or metastatic disease (see Appendix for trial details). A summary of the common tumors and their reported median survival is shown in Table 3.

For patients with an anticipated survival of 6 months or more, survival data from recent trials provides little more than general information about prognosis. What factors help refine prognosis for these patients? Prognostic modifiers for patients felt to have 'chronic' metastatic disease include: performance status, hypercalcemia, brain metastases, and pleural effusions.

Hypercalcemia

Hypercalcemia is one of the most common metabolic complications of cancer and usually occurs during the last weeks of life. A review of the effects of anti-hypercalcemic treatment on morbidity and mortality in cancer-associated hypercalcemia reported a median survival of 30 days.[25] For the subset of patients for whom specific therapeutic interventions were directed at the cancer, survival was improved to 135 days. These data predate the widespread use of bisphosphonates for patients with osteolytic bone metastases from solid tumors. The poor prognosis for hypercalcemia does not appear to have changed, though anecdotally, its incidence is reduced.

Table 3: Survival of adult patients receiving antineoplastic therapy

Tumor site	Disease status	Median survival (months)
Bladder (TCC)	Advanced/metastatic	9−15
Brain – glioblastoma multiforme	Newly diagnosed	10−11
Breast	Metastatic	15−22
Cervix – squamous	Recurrent	6−8
Colorectal	Advanced/metastatic	12−22
Esophagus	Advanced/metastatic	3−6
Gastric	Advanced	7
Head and neck	Advanced/recurrent	5−12
Kidney	Metastatic	12−13
Liver	Advanced	3−10
Non small-cell lung cancer	Advanced	6−11
Small cell lung cancer	Extensive	9−14
Melanoma	Metastatic	5−12
Ovarian	Advanced	10−36
Pancreas	Advanced	5−6
Prostate	Refractory	9−14
Sarcoma	Advanced	12−14
Unknown primary	Metastatic	8−13

Brain metastases

The incidence of brain metastases has increased as treatment options for systemic disease have improved. In addition, a multimodal approach to brain metastases can prolong survival in some patients, though for the majority, this is a life-limiting site of metastases. Gaspar et al. analyzed 1,200 patients enrolled in 3 consecutive RTOG brain metastases trials to identify prognostic factors for survival.[26] Using recursive partitioning analysis, best survival (median 7.1 months) was observed in patients <65 years old with a Karnofsky performance scale ≥70 and controlled primary tumor; worst survival (median 2.3 months) was observed in patients with a Karnofsky performance scale <70 (Group 3). All other patients fell into an intermediate prognostic group with a median survival of 4.2 months (Group 2). When a similar analysis was applied to patients who underwent surgical resection of brain metastases (with or without radiotherapy), the overall survival

was improved.[27] However, the survival varied based on the patient characteristics defined by the 3 groups, with a median survival of groups 1, 2, and 3 of 14.8, 9.9, and 6 months, respectively. In a highly selected group of patients, those with a Karnofsky performance scale >70 and the absence of extracranial disease, prolonged survival (>1 year) can be anticipated.

Malignant pleural effusions

Symptomatic malignant pleural effusions generally portend a poor prognosis, with a median survival of less than 4 months.[28, 29] As with other manifestations of advanced disease, prognosis is modified by Karnofsky performance scale.[29] Patients with recurrent, symptomatic pleural effusions and a Karnofsky performance scale score of ≥70 have a median survival of 13 months, while those with a Karnofsky performance scale ≤30 have a median survival of 1 month. While some series have failed to identify primary tumor site as a significant prognostic variable, others note a markedly worse survival for patients with non-small cell lung cancer and a malignant effusion (median survival 2.9 months) and a better outcome for those with breast cancer (median survival 10 months) or ovarian cancer (median survival 9 months).[28,,30]

There is inadequate data to provide accurate prognostic information for most patients with metastatic disease and months to years of projected survival. However, when complications such as hypercalcemia or brain metastases occur, among others, the prognosis can be more clearly defined and inform both treatment and personal decisions.

6-steps for clarifying diagnosis and prognosis

It is difficult to predict prognosis for an individual patient, and it can be difficult to present this information.

This module adapts the 6-step protocol, SPIKES, presented in EPEC-O Module 7: Communicating Effectively, to guide the communication and clarification of diagnosis and prognosis.[31,32,33]

During the first 3 steps, prepare to share the information. Start by gathering the facts. Then sit down comfortably and assess the patient's understanding. Inquire what the patient knows, and what s/he would like to know about the diagnosis and/or prognosis.

Some of these first 3 steps can be completed before the session at which the physician actually discusses the news.

During the last 3 steps, manage the information carefully. Deliver the news clearly, succinctly and without using jargon. Once the facts have been stated, stop talking. Give time for the patient's reactions and respond to them. Once the patient is settled, plan for follow-up.

SPIKES	6-step protocol to clarify diagnosis and prognosis
Setting. Getting started.	1. Getting started.
Perception. What does the patient know?	2. What does the patient know?
Invitation. How much does the patient want to know?	3. How much does the patient want to know?
Knowledge. Sharing the information.	4. Share the information.
Emotion. Responding to feelings.	5. Respond to feelings.
Subsequent. Planning and follow-up.	6. Plan next steps and follow-up.

Don't consider this protocol to be a script to be followed rigorously. Use it as a tool to guide important aspects of an interaction in which difficult information is shared.

Step 1: Getting started

Before starting to communicate any news, plan what will be discussed. Confirm the medical facts of the case, ie, the diagnosis, prognosis, etc. Ensure that all the needed information is available. If this is an unfamiliar task, rehearse what you will say. Don't delegate the task. If several team members will be present, it may be helpful for the team to meet to plan the communication in advance.

Create an environment conducive to effective communication. Ensure privacy and adequate seating. Ensure that a box of facial tissues is handy and a glass of water.

Allot adequate time for the discussion. Do not slip this into a short interval between other critical tasks. Prevent interruptions. Arrange to hold telephone calls and pages.

Determine who else the patient would like to have present for the discussion. This might include family, significant others, surrogate decision makers, and/or key members of the interdisciplinary team, eg, nurse, social worker, chaplain, etc.

Step 2: What does the patient know?

Start the discussion by establishing what the patient and family know about the patient's health. With this information, ascertain if the patient and family will be able to comprehend the information.

Questions might include:

- What do you understand about your diagnosis and its prognosis?
- How would you describe the change in your medical situation?
- Have you been worried about your illness or treatment?
- What did you think is causing symptom x?
- When you developed new symptoms, what did you think might be going on?
- What are your expectations from treatment?
- Did you think something serious was going on when you developed new symptoms?
- How do you expect your diagnosis to effect your survival?

Occasionally a patient will fall silent and seem completely unprepared or unable to respond. To ease the situation and stimulate discussion, try to clarify what the patient understands about his or her medical history and recent investigations. Identify absent family members or others on whom the patient relies. If this is ineffective and the patient remains silent, or if it appears the patient requires more support, it may be better to reschedule the meeting for another time.

Step 3: How much does the patient want to know?

Next, establish what and how much each patient wants to know.

People handle information differently, depending on their race, ethnicity and culture, religion, and socioeconomic class. Each person has the right to voluntarily decline to receive any information and may designate someone else to communicate on his or her behalf. Ask the patient and family how they would like to receive information. If the patient prefers not to receive critical information, establish who to give information to.

Possible questions include the following:

- If the tests turn out to show something serious, do you want to know?
- Are you the kind of person who likes to know all the facts?
- Would you like me to tell you the full details of your treatment and prognosis? If not, is there somebody else you would like me to talk to?

- Some people really do not want to be told how the cancer will effect survival, but would rather their families be told instead. What do you prefer?
- Do you want me to go over the anticipated results of the treatment now, and explain exactly how I think it will affect you?
- Who would you like me to talk to about these issues?

Before introducing the subject of prognosis, or directly answering their questions about prognosis, consider starting with questions like:

- Many patients want to know the prognosis. Is this true for you?
- What are you expecting to happen?
- How specific do you want me to be?
- What experiences have you had with others with cancer?
- What experiences have you had with others who have died?
- What are you afraid will happen?

The way the patient answers the questions will give clues to her/his educational level, verbal fluency, and family dynamics. Listen carefully and observe everyone's responses to your questions. Use this experience to influence how you deliver your news.

Advance preparation

All of the discussion to this point is about preparation to give the diagnosis and prognosis. Some of that preparation might best occur well before the information is actually given. The initial assessment, and subsequent discussions that prepare the patient for critical tests, all provide opportunities to determine what the patient already knows and how he or she would like to have information handled.

Provide periodic information and cautions that the news might not always be good. With this incremental approach and periodic 'warning shots,' the patient and family may be better prepared for 'bad' news.

When the family says 'don't tell'

Many times, family members will ask the physician not to tell the patient the diagnosis, prognosis or other important information. While it is the physician's legal obligation to obtain informed consent from the patient, an effective therapeutic relationship requires a congenial alliance with the family.

Rather than confronting their request with, 'I have to tell the patient,' inquire why they are concerned. Possible questions include:

- Why don't you want me to tell the patient?

- What is it that you are afraid I will say?
- Tell me about your past experience with cancer?
- Is there a personal, cultural, or religious context that I should know about?

Suggest that you go to the patient together to ask how much s/he wants to know about her/his health and what questions there might be. Share anecdotes, talk about the pain of secrecy and the opportunities that come with open communication.

These situations may require significant negotiation. In particularly difficult cases, support from the institutional ethics committee may be very helpful. Ultimately, it may be decided, after discussion with the patient, that details of diagnosis and prognosis and treatment decisions will be discussed only with the family. However, unless the patient has previously indicated that he or she wants no information, hiding the diagnosis or important information about prognosis or treatment from the patient is neither ethical nor legally acceptable.

There are ethnic and cultural differences in the preferred handling of information. While knowledge of such differences is useful as a background, global conclusions about them rarely help with decision making for an individual. Ask a patient about general preferences for handling of medical information and decision making early in the clinical relationship before significant information needs to be shared. This will help the clinician to avoid making a misstep.

Step 4: Share the information

Before sharing the information, consider the implications of the prognostic information you provide. Patients who wish to plan their lives want information that is more detailed. Those who are terrified may do better with answers that are more general. Definitive answers, eg, 'You will be cured,' or 'You have 6 months to live,' run the risk of producing disappointment if the time proves to be less, and anger or frustration if you had underestimated the patient's lifespan.

Consider responding by giving a range of time that encompasses an average life expectancy, such as 'hours to days,' 'days to weeks,' 'weeks to months,' 'months to years,' etc. Alternatively, indicate averages such as 'one-third of people will be alive and well a year from now, half will live about 6 months. Exactly what will happen for you, I don't know.' After giving a range, it may help to emphasize the limits of prediction by saying something like, 'What this will mean for you I can't tell. We need to hope for the best, while we plan for the worst. We can't predict surprises and should plan in case something happens. We'll have a better sense over time how things will evolve for you.'

Once you are ready, deliver the information in a sensitive but straightforward manner.

Start by letting the patient know that you have news, then share the facts about the patient's diagnosis and prognosis. Say it, then stop. Avoid delivering all of the

information in a single, steady monologue. Use simple language that is easy to understand. Avoid technical jargon or euphemisms. Pause frequently. Check for understanding. Use silence and body language as tools to facilitate the discussion.

Do not minimize the severity of the situation. Well-intentioned efforts to 'soften the blow' may lead to vagueness and confusion.

You might choose to tell the diagnosis and prognosis by using language like:

- I feel badly to have to tell you this, but your cancer has recurred and you only have a few months left to live.
- I'm afraid the news is not good. The CT showed that your colon cancer has spread to your liver. This is a treatable, but not curable disease.
- Unfortunately, there's no question about the CT scan: the cancer has spread to your liver.
- The report is back, and it's not as we had hoped. It showed that there is cancer in your liver. I'm afraid this is not curable disease.
- I'm afraid I have bad news. The CT scan shows your husband has cancer throughout his liver.

I'm Sorry

The phrase 'I'm sorry may be interpreted to imply that the physician is responsible for the situation. It may also be misinterpreted as pity or aloofness. If you use the phrase, adjust it to show empathy. For example, 'I'm sorry to have to tell you this.' The phrase, 'I wish things were different' may be equally effective at communicating empathy without conveying responsibility for the condition.[34]

Step 5: Respond to feelings

Patients and families respond to bad news in a variety of ways. Some respond emotionally with tears, anger, sadness, love, anxiety, relief, or other strong emotions. Others experience denial, blame, guilt, disbelief, fear, or a sense of loss or shame, or may even intellectualize why the situation is happening. A few may demonstrate reflexive psychophysiologic responses such as 'fight or flight' and may even try to bolt from the room or totally withdraw into themselves.

Outbursts of strong emotion make many oncologists and other physicians uncomfortable.[35] Give the patient and family time to react. Be prepared to support them through a broad range of reactions.

Listen quietly and attentively. Acknowledge their emotions. Ask them to describe their feelings:

- I imagine this is difficult news…

- You appear to be angry. Can you tell me what you are feeling?
- Does this news frighten you?
- Tell me more about how you are feeling about what I just said.
- What worries you most?
- What does this news mean to you?
- I wish the news were different.
- I'll try to help you.
- Is there anyone you would like for me to call?
- I'll help you tell your son.

Remind them that their responses are normal. Make a box of facial tissue available. Nonverbal communication may also be very helpful. Consider touching the patient in an appropriate, reassuring manner. Offer a drink of water, a cup of tea, or something else that might be soothing.

Allow time for the patient and family to express all of their immediate feelings. Don't rush them. Once the emotion is 'spent,' most people will be able to move on. This usually last only a few minutes. The most frequent physician error is to talk.[36] Yet, this is counter-productive. A shared understanding of the news and its meaning enhances the physician-patient relationship and facilitates future decision making and planning.

Step 6: Plan next steps and follow-up

Establish a plan for the next steps. This may include gathering additional information or performing further tests. Treat current symptoms. It may include helping parents to tell their child about their illness and what treatment will be like for them. Arrange for appropriate referrals. Explain plans for additional treatment. Discuss potential sources of emotional and practical support, eg, family, significant others, friends, social worker, spiritual counselor, peer support group, professional therapist, hospice, home health agency, etc.

Always caution patients and families that unexpected surprises can happen. Suggest that they get their affairs in order so they won't be vulnerable if something unexpected does occur. Reassure them that you will be available to them to deal with issues and support them throughout their illness, whatever happens. Help clarify what can be realistically expected and distinguish this from what might be wished for or what is most feared. Identify the miraculous for what it is—something outside of usual experience that happens exceedingly rarely.

Reassure the patient and family that they are not being abandoned and that the physician will be actively engaged in an ongoing plan to help. Indicate how the patient and family

can reach the physician to answer additional questions. Establish a time for a follow-up appointment.

Ensure that the patient will be safe when he or she leaves. Is the patient able to drive home alone? Is the patient distraught, feeling desperate, or suicidal? Is there someone at home to provide support?

At future visits, elements of this protocol may need to be revisited. Many patients and families require repetition of the news to gain a complete understanding of their situation.

Unrealistic expectations

Despite the communication of accurate information, a survey of surgical, medical, pediatric, and radiation oncologists showed that 29% thought patient's unrealistic expectations were a challenge. 50% thought family's unrealistic expectations were a challenge.

Apply the 6-step protocol in cases where unrealistic expectations are expressed. In particular, focus on step 2.

- What is it that the patient and family know?
- What are they expecting?
- What have they heard the oncologist say?
- What other information do they have?

Try to 'suspend belief' and form a mental image of the patient's or family's point of view. What may have initially appeared to be an unrealistic expectation may seem less bizarre once the point of view is understood.

A frequent occurrence is that a difference in values, ie, 'it's important to try anything, no matter how small the chance' or 'it's important to be a fighter,' will emerge. Differences in values are not resolved by scientific data.

Once a common understanding is developed, explore how the conflict can be resolved. This is discussed more in EPEC-O Module 12: Conflict Resolution.

Summary

The 6-step protocol for communicating effectively (see EPEC-O Module 7: Communicating Effectively) provides a tool to guide the communication and confirmation of diagnosis and prognosis.

Prognostication is an inexact science, and physicians are often overly optimistic with their survival estimates. There are multiple sources of prognostic information, eg, clinician estimates of survival, signs and symptoms, Karnofsky performance scale, stage-specific survival data, and integrated modules. Karnofsky performance scale is an

independent prognostic factor highly predictive of survival when the Karnofsky performance scale is under 50. For patients with very advanced disease and an anticipated survival of less than 3 months, some symptoms, eg, dyspnea, are highly predictive of survival less than 1 month.

Prognosis is more difficult to predict for patients with advanced disease and a longer anticipated survival. Some cancer complications redefine prognosis for this group. There remains inadequate prognostic information for many of these patients and further research is needed.

Key take-home points

1. Physicians are often overly optimistic with their survival estimates.
2. Inquire why the patient and family are asking about prognosis in order to have a sense of their context for the question.
3. Give as accurate as estimate of prognosis as you can, when requested.
4. The 6 step protocol for communicating effectively provides a tool for clarification of diagnosis and prognosis.

Pearls

1. The shorter the anticipated survival, the more accurate physician predictions of survival tend to be.
2. Hypercalcemia, pleural effusions, and brain metastasis portend a poor prognosis.

Pitfalls

1. If you try to ‘soften the blow,’ the patient and family may not understand the significance of the message.
2. Clarify terms: be sure patients and families understand how ‘response’ does and does not relate to cure.

Appendix: Survival of adult patients by type of cancer in phase III trials

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
Bladder	Transitional Cell		9				Popov I, Jelic S, Radosavljevic D, Nikolic-Tomasevic Z. Amsacrine and cisplatin in poor prognosis patients with metastatic transitional cell carcinoma of the urothelium: a phase-II study. Eur Urol. 2001 Sep;40(3):324-9. PMID: 11684850. Full Text	
			15 / 14		35 / 25		Sternberg CN, de Mulder PH, Schornagel JH, Theodore C, Fossa SD, van Oosterom AT, Witjes F, Spina M, van Groeningen CJ, de Balincourt C, Collette L; European Organization for Research and Treatment of Cancer Genitourinary Tract Cancer Cooperative Group. Randomized phase III trial of high-dose-intensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer Protocol no. 30924. J Clin Oncol. 2001 May 15;19(10):2638-46. PMID: 11352955. Full Text	
			14 / 15	58			von der Maase H, Hansen SW, Roberts JT, Dogliotti L, Oliver T, Moore MJ, Bodrogi I, Albers P, Knuth A, Lippert CM, Kerbrat P, Sanchez Rovira P, Wersall P, Cleall SP, Roychowdhury DF, Tomlin I, Visseren-Grul CM, Conte PF. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: results of a large, randomized, multinational, multicenter, phase III study. J Clin Oncol. 2000 Sep;18(17):3068-77. PMID: 11001674. Full Text	
Brain	Glioblastoma multiforme (GBM)	Newly diagnosed	11 / 11	45 / 44			Grossman SA, O'Neill A, Grunnet M, Mehta M, Pearlman JL, Wagner H, Gilbert M, Newton HB, Hellman R; Eastern Cooperative Oncology Group. Phase III study comparing three cycles of infusional carmustine and cisplatin followed by radiation therapy with radiation therapy and concurrent carmustine in patients with newly diagnosed supratentorial glioblastoma multiforme: Eastern Cooperative Oncology Group Trial 2394. J Clin Oncol. 2003 Apr 15;21(8):1485-91. PMID: 12697871. Full Text	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
		Newly diagnosed	11 / 11				Buckner JC, Schomberg PJ, McGinnis WL, Cascino TL, Scheithauer BW, O'Fallon JR, Morton RF, Kuross SA, Mailliard JA, Hatfield AK, Cole JT, Steen PD, Bernath AM. A phase III study of radiation therapy plus carmustine with or without recombinant interferon-alpha in the treatment of patients with newly diagnosed high-grade glioma. Cancer. 2001 Jul 15;92(2):420-33. PMID: 11466698. Full Text	
		Newly diagnosed	10 / 10.5				Prados MD, Wara WM, Sneed PK, McDermott M, Chang SM, Rabbitt J, Page M, Malec M, Davis RL, Gutin PH, Lamborn K, Wilson CB, Phillips TL, Larson DA. Phase III trial of accelerated hyperfractionation with or without difluromethylornithine (DFMO) versus standard fractionated radiotherapy with or without DFMO for newly diagnosed patients with glioblastoma multiforme. Int J Radiat Oncol Biol Phys. 2001 Jan 1;49(1):71-7. PMID: 11163499. Full Text	
Breast	Adeno-carcinoma	IV	17.4 / 16				Milla-Santos A, Milla L, Portella J, Rallo L, Pons M, Rodes E, Casanovas J, Puig-Gali M. Anastrozole versus tamoxifen as first-line therapy in postmenopausal patients with hormone-dependent advanced breast cancer: a prospective, randomized, phase III study. Am J Clin Oncol. 2003 Jun;26(3):317-22. PMID: 12796608. Full Text	ER+
		IV	1.7 yr				Parnes HL, Cirrincione C, Aisner J, Berry DA, Allen SL, Abrams J, Chuang E, Cooper MR, Perry MC, Duggan DB, Szatrowski TP, Henderson IC, Norton L; Cancer and Leukemia Group B. Phase III study of cyclophosphamide, doxorubicin, and fluorouracil (CAF) plus leucovorin versus CAF for metastatic breast cancer: Cancer and Leukemia Group B 9140. J Clin Oncol. 2003 May 1;21(9):1819-24. PMID: 12721259. Full Text	
		IV	18.9 / 22.2				Sledge GW, Neuberg D, Bernardo P, Ingle JN, Martino S, Rowinsky EK, Wood WC. Phase III trial of doxorubicin, paclitaxel, and the combination of doxorubicin and paclitaxel as front-line chemotherapy for metastatic breast cancer: an intergroup trial (E1193). J Clin Oncol 2003 Feb 15;21(4):588-92. Sledge GW, Neuberg D, Bernardo P, Ingle JN, Martino S, Rowinsky EK, Wood WC. Phase III trial of doxorubicin, paclitaxel, and the combination of doxorubicin and paclitaxel as front-line chemotherapy for metastatic breast cancer: an intergroup trial (E1193). J Clin Oncol. 2003 Feb 15;21(4):588-92. PMID: 12586793. Full Text	

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Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
		IV	16 / 15				Bonneterre J, Roche H, Monnier A, Guastalia JP, Namer M, Fargeot P, Assadourian S. Docetaxel vs 5-fluorouracil plus vinorelbine in metastatic breast cancer after anthracycline therapy failure. Br J Cancer. 2002 Nov 18;87(11):1210-5. PMID: 12439707. Full Text	Second-line therapy
		IV	22.5 / 21.7				Nabholtz JM, Falkson C, Campos D, Szanto J, Martin M, Chan S, Pienkowski T. Docetaxel and doxorubicin compared with doxorubicin and cyclophosphamide as first-line chemotherapy for metastatic breast cancer: results of a randomized, multicenter, phase III trial. J Clin Oncol. 2003 Mar 15;21(6):968-75. PMID: 12637459. Full Text	
Cervix	Squamous Cell	IV	8 / 6				Kumar L, Pokharel YH, Kumar S, Singh R, Rath GK, Kochupillai V. Single agent versus combination chemotherapy in recurrent cervical cancer. J Obstet Gynaecol Res. 1998 Dec;24(6):401-9. PMID: 10063235.	
Colorectal	Adeno-carcinoma	IV	22 / 21				J Clin Oncol 2004 Jan 15;22(2):229-37. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study. Tournigand C, Andre T, Achille E, Lledo G, Flesh M, Mery-Mignard D, Quinaux E, Couteau C, Buyse M, Ganem G, Landi B, Colin P, Louvet C, de Gramont A.	
		IV	11 / 13 / 13				J Clin Oncol 2003 Oct 15;21(20):3721-8. Randomized phase III study of high-dose fluorouracil given as a weekly 24-hour infusion with or without leucovorin versus bolus fluorouracil plus leucovorin in advanced colorectal cancer: European Organization of Research and Treatment of Cancer Gastrointestinal Group Study 40952. Kohne CH, Wils, J, Lorenz M, Schoffski P, Voigtmann R, Bokemeyer C, Lutz M, Kleeberg C, Ridwelski K, Souchon R, El-Serafi M, Weiss U, Burkhard O, Ruckle H, Lichnitser M, Langenbuch T, Scheithauer W, Baron B, Couvreur ML, Schmoll HJ: European Organization of Research and Treatment of Cancer Gastrointestinal Group Study 40952.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
		IV	13 / 12				J Clin Oncol 2001 Nov 1;19(21):4097-5106. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: results of a large phase III study. Van Cutsem E, Twelves C, Cassidy J, Allman D, Bajetta E, Boyer M, Bugat R, Findlay M, Frings S, Jahn M, McKendrick J, Osterwalder B, Perez-Manga G, Rosso R, Rougier P, Schmiegel WH, Seitz JF, Thompson P, Vieitez JM, Weitzel C, Harper P: Xeloda Colorectal Cancer Study Group.	
Esophagus		IV	4				Oncology 2003 Sep;17(9 Suppl 8):27-31. Phase II study of docetaxel and irinotecan in metastatic or recurrent esophageal cancer: a preliminary report. Govindan R, Read W, Faust J, Trinkaus K, Ma MK, Baker SD, McLeod HL, Perry MC.	
		IV	6				Int J Colorectal Dis 2003 Jul;18(4):330-4. A pilot study of irinotecan (CPT-11) as single-agent therapy in patients with locally advanced or metastatic esophageal carcinoma. Muhr-Wilkenshoff F, Hinkelbein W, Ohnesorge I, Wolf KJ, Riecken EO, Zeitz M.	
		IV	3				Invest New Drugs 2000 May;18(2):199-202. A phase II trial of topotecan in esophageal carcinoma: a Southwestern Oncology Group study (SWOG 9339). Macdonald JS, Jacobson JL, Ketchel SJ, Weiss G, Taylor S, Mills G, Kuebler JP, Rivkin S, Conrad M.	
		IV	6				Eur J Cancer 1994;30A(3):325-8. 5-Fluorouracil, folinic acid, etoposide and cisplatin chemotherapy for locally advanced or metastatic carcinoma of the oesophagus. Stahl M, Wilke H, Meyer HJ, Preusser P, Berns T, Fink U, Achterrath W, Knipp H, Harstick A, Berger M, et al.	
Gastric	Adeno-carcinoma	IV	7 / 7 / 7				J Clin Oncol 2000 Jul;18(14):2648-57. Final results of a randomized phase III trial of sequential high-dose methotrexate, fluorouracil, and doxorubicin versus etoposide, leucovorin, and fluorouracil versus infusional fluorouracil and cisplatin in advanced gastric cancer: a trial of the European Organization for Research and Treatment of Cancer Gastrointestinal Tract Cancer Cooperative Group. Vanhoefer U, Rougier P, Wilke H, Ducreux MP, Lacave AJ, Van Cutsem E, Planker M, Santos JG, Piedbois P, Paillot B, Bodenstein H, Schmoll HJ, Bleiberg H, Nordlinger B, Couvreur ML, Baron B, Wils JA.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
Head and neck	Squamous Cell	IV	7	29			J Clin Oncol 2001 Feb 15;19(4):1088-95. Phase III comparison of high-dose paclitaxel + cisplatin + granulocyte colony-stimulating factor versus low-dose paclitaxel + cisplatin in advanced head and neck cancer: Eastern Cooperative Oncology Group Study E1393. Forastiere AA, Leong T, Rowinsky E, Murphy BA, Vlock DR, DeConti RC, Adams GL.	Unresectable, recurrent or metastatic
			12				Cancer 2002 Apr 15;94(8):2224-31. Phase II study of methotrexate, vinblastine, doxorubicin, and cisplatin in patients with squamous cell carcinoma of the upper respiratory and alimentary passages of the head and neck. Okuno SH, Mailliard JA, Suman VJ, Edmonson JH, Creagan ET, Nair S, Levitt R, Kugler JW.	
			5 / 8	26 / 33			J Clin Oncol 2004 Jan 15;22(2):262-8. Outcome of elderly patients with recurrent or metastatic head and neck cancer treated with cisplatin-based chemotherapy. Argiris A, Li Y, Murphy BA, Langer CJ, Forastiere AA.	
Kidney	Carcinoma	IV	13 / 12	55 / 47			J Clin Oncol 1999 Aug;17(8):2521-9. Multicenter, randomized, phase III trial of CD8(+) tumor-infiltrating lymphocytes in combination with recombinant interleukin-2 in metastatic renal cell carcinoma. Figlin RA, Thompson JA, Bukowski RM, Vogelzang NJ, Novick AC, Lange P, Steinberg GD, Belldegrun AS.	
Liver	Hepatocellular carcinoma		10 / 3				Hepatogastroenterology 1998 Nov-Dec;45(24):1955-60. Biochemical modulation of doxorubicin by high-dose tamoxifen in the treatment of advanced hepatocellular carcinoma. Cheng AL, Yeh KH, Fine RL, Chuang SE, Yang CH, Wang LH, Chen DS.	
Lung	Non-small cell	IIIb / IV	10 / 9	45 / 35			Br J Cancer 2003 Oct 6;89(7):1192-9. First-line gemcitabine with cisplatin or epirubicin in advanced non-small-cell lung cancer: a phase III trial. Wachters FM, Van Putten JW, Kramer H, Erjavec Z, Eppinga P, Strijbos JH, de Leede GP, Boezen HM, de Vries EG, Groen HJ.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
		IIIb / IV	11 / 11		21 / 14		J Clin Oncol 2003 Aug 15;21(16):3016-24. Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: the TAX 326 study group. Fossella F, Pereira JR, von Pawel J, Pluzanska A, Gorbounova V, Kaukel E, Mattson KV, Ramlau R, Szczesna A, Fidias P, Millward M, Belani CP.	
		IIIb / IV	9 / 7	38 / 28			J Natl Cancer Inst 2003 Mar 5;95(5):362-72. Chemotherapy for elderly patients with advanced non-small-cell lung cancer: the Multicenter Italian Lung Cancer in the Elderly Study (MILES) phae III randomized trial. Gridelli C, Perrone F, Gallo C, Cigolari S, Rossi A, Piantedosi F, Barbera S, Ferrau F, Piazza E, Rosetti F, Clerici M, Bertetto O, Robbiati SF, Frontini L, Sacco C, Castiglione F, Favaretto A, Novello S, Migliorino MR, Gasparini G, Galetta D, Laffaioli RV, Gebbia V: MILES Investigators.	
		IIIb / IV	9 / 8	24 / 20			Lung Cancer 2003 Feb;39(2):179-89. Gemcitabine and cisplatin versus vinorelbine and cisplatin versus ifosfamide + gemcitabine followed by vinorelbine and cisplatin versus vinorelbine and cisplatin followed by ifosfamide and gemcitabine in stage IIIB-IV non small cell lung carcinoma: a prospective randomized phase III trial of the Gruppo Oncologico Italia Meridionale. Gebbia V, Galetta D, Caruso M, Verderame F, Pezzella G, Valdesi M, Borsellino N, Pandolfo G, Durini E, Rinaldi M, Loizzi M, Gebbia N, Valenza R, Tierrito ML, Varvara F, Colucci G: Gruppo Oncologico Italia Meridionale.	
		IV	6 / 8 / 8	23 / 33 / 35	11 / 14 / 17		Ann Oncol 2002 Jun;13(6):874-82. A three-arm phase III randomised trial comparing combinations of platinum derivatives, ifosfamide and / or gemcitabine in stage IV non-small-cell lung cancer. Sculier JP, Lafitte JJ, Lecomte J, Berghmans T, Thiriaux J, Florin MC, Efremidis A, Alexopoulos CG, Recloux P, Ninane V, Memmen P, Paesmans M, Klastersky J: European Lung Cancer Working Party.	
Lung	Small cell		14 / 10		14 / 6	5 / 2	J Clin Oncol 2002 Dec 15;20(24):4665-72. Cisplatin and etoposide regimen is superior to cyclophosphamide, epirubicin, and vincristine regimen in small-cell lung cancer: results from a randomized phase III trial with 5 years' follow-up. Sundstrom S, Bremnes RM, Kaasa S, Aasebo U, Hatlevoll R, Dahle R, Boye N, Wang M, Vigander T, Vilsvik J, Skovlund E, Hannisdal E, Aamdal S: Norwegian Lung Cancer Study Group.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
			10	28 / 25			J Clin Oncol 2001 Apr 15;19(8):2114-22. Topotecan versus observation after cisplatin plus etoposide in extensive-stage small-cell lung cancer: E7593—a phase III trial of the Eastern Cooperative Oncology Group. Schiller JH, Adak S, Cella D, DeVore RF.	
			10 / 9	40 / 29			J Natl Cancer Inst 2001 Feb 21;93(4):300-8. Etoposide plus cisplatin with or without the combination of 4'-epidoxorubicin plus cyclophosphamide in treatment of extensive small-cell lung cancer: a French Federation of Cancer Institutes multicenter phase III randomized study. Pujol JL, Daures JP, Riviere A, Quoix E, Westeel V, Quantin X, Breton JL, Lemarie E, Poudenx M, Milleron B, Moro D, Debieuvre D, Le Chevalier T.	
			12 / 11	51 / 40	16 / 7		Ann Oncol 2002 Jan;13(1):95-102. Maintenance daily oral etoposide versus no further therapy following induction chemotherapy with etoposide plus ifosfamide plus cisplatin in extensive small-cell lung cancer: a Hoosier Oncology Group randomized study. Hanna NH, Sandier AB, Loehrer PJ Sr, Ansari R, Jung SH, Lane K, Einhorn LH.	
Melanoma			12 / 9				J Clin Oncol 2002 Apr 15;20(8):2045-52. Sequential biochemotherapy versus chemotherapy for metastatic melanoma: results from a phase III randomized trial. Eton O, Legha SS, Bedikian AY, Lee JJ, Buzaid AC, Hodges C, Ring SE, Papadopoulos NE, Plager C.	
			8 / 6				J Clin Oncol 2000 Jan;18(1):158-66. Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. Middleton MR, Grob JJ, Aaronson N, Fierlbeck G, Tilgen W, Seiter S, Gore MA.	
			7	25			Cancer 1999 May 1;85(9):1979-84. A phase III randomized trial of dacarbazine and carboplatin with and without tamoxifen in the treatment of patients with metastatic melanoma. Agarwala SS, Ferri W, Gooding W, Kirkwood JM.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
			9				J Clin Oncol 1998 May;16(5):1743-51. Phase III trial of dacarbazine versus dacarbazine with interferon alpha-2b versus dacarbazine with tamoxifen versus dacarbazine with interferon alpha-2b and tamoxifen in patients with metastatic malignant melanoma: an Eastern Cooperative Oncology Group study. Falkson CI, Ibrahim J, Kirkwood JM, Coates AS, Atkins MB, Blum RH.	
			5 / 9				J Clin Oncol 2002 Jan 1;20(1):125-33. Results from a randomized phase III study comparing combined treatment with histamine dihydrochloride plus interleukin-2 versus interleukin-2 alone in patients with metastatic melanoma. Agarwala SS, Glaspy J, O'Day SJ, Mitchell M, Gutheil J, Whitman E, Gonzalez R, Hersh E, Feun L, Belt R, Meyskens F, Hellstrand K, Wood D, Kirkwood JM, Gehlsen KR, Naredi P.	
			10 / 11				J Clin Oncol 2002 Mar 15;20(6):1600-7. Cisplatin, dacarbazine with or without subcutaneous interleukin-2, and interferon alpha-2b in advanced melanoma outpatients: results from an Italian multicenter phase III randomized clinical trial. Ridolfi R, Chi.	
Myeloma		Relapsed	31				Biol Blood Marrow Transplant 2000;6(4A):448-55. Treat-ment of primary resistant or relapsed multiple myeloma with high-dose chemoradiotherapy, hematopoietic stem cell rescue, and granulocyte-macrophage colony-stimulating factor. Schenkein DP, Koc Y, Alcindor T, Stadtmauer EA, Miller KB, Cooper BW, Partridge AH, Lazarus HM.	
Ovarian	Adeno-carcinoma		10				J Clin Oncol 2003 Jan 15;21(2):291-7. Phase II trial of irinotecan in patients with metastatic epithelial ovarian can-cer or peritoneal cancer. Bodurka DC, Levenback C, Wolf JK, Gano J, Wharton JT, Kavanagh JJ, Gershenson DM.	
			15				Gynecol Oncol 2003 Sep;90(3):581-6. Cisplatin as second-line therapy in ovarian carcinoma treated initially with single-agent paclitaxel: a Gynecologic Oncology Group Study. Thigpen JT, Blessing JA, Olt G, Lentz SS, Bell J.	Progressive, persistent after first-line treatment

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
			36 / 26				J Natl Cancer Inst 2000 May 3;92(9):699-708. Randomized intergroup trial of cisplatin-paclitaxel versus cisplatin-cyclophosphamide in women with advanced epithelial ovarian cancer: three-year results. Piccart MJ, Bertelsen K, James K, Cassidy J, Mangio.	
			27 / 18				J Clin Oncol 2001 Jul 15;19(4):3312-22. Recurrent epithelial ovarian carcinoma: a randomized phase III study of pegylated liposomal doxorubicin versus topotecan. Gordon AN, Fleagle JT, Guthrie D, Parkin DE, Gore ME, Lacave AJ.	
			13 / 12				J Clin Oncol 2003 Aug 1;21(15):2843-8. Phase III trial of paclitaxel at two dose levels, the higher dose accompanied by filgrastim at two dose levels in platinum-pretreated epithelial ovarian cancer: an intergroup study. Omura GA, Brady MJ, Look KY, Ave.	
		III / IV	24				Gynecol Oncol 2003 Oct;91(1):902-10. Gemcitabine combined with cisplatin as first-line treatment in patients with epithelial ovarian cancer: a phase II study. Belpomme D, Krakowski I, Beauduin M, Petit T, Canon JL, Janssens J, Gauthier S, De Pauw A, Moreau V, Kayitalire L.	
Pancreas	Adeno-carcinoma	IV	5 / 6				Cancer 2002 Feb 15;94(4):902-10. Gemcitabine alone or with cisplatin for the treatment of patients with locally advanced and / or metastatic pancreatic carcinoma: a prospective, randomized phase III study of the Gruppo Oncologia dell'Italia Meridionale. Colucci G, Giuliani F, Gebbia V, Biglietto M, Rabitti P, Uomo G, Cigolari S, Testa A, Maiello E, Lopez M.	
Prostate (hormone refractory)	Adeno-carcinoma	IV	12 / 14				Cancer 2002 Feb 1;94(3):665-72. Higher doses of mitoxantrone among men with hormone-refractory prostate carcinoma: a Cancer and Leukemia Group B study. Levine EG, Halabi S, Roberts JD, Kaplan EB, Rago R, Atkins JN, Vogelzang NJ.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2 or 3 arms of the phase III trial'								
		IV	10 / 9				J Clin Oncol 2000 Apr;18(7):1440-50. Suramin therapy for patients with symptomatic hormone-refractory prostate cancer: results of a randomized phase III trial comparing suramin plus hydrocortisone to placebo plus hydrocortisone. Small EJ, Meyer M, Marshall ME, Reyno LM, Meyers FJ, Natale RB, Lenehan PF, Chen L, Slichenmyer WJ, Eisenberger M.	
Sarcoma	Soft tissue	IV	14 / 14	53 / 57	24 / 26		J Clin Oncol 2000 Jul;18(14):2676-84. Randomized phase III study comparing conventional-dose doxorubicin plus ifosfamide versus high-dose doxorubicin plus ifosfamide plus recombinant human granulocyte-macrophage colony-stimulating factor in advanced soft tissue sarcomas: a trial of the European Organization for Research and Treatment of Cancer / Soft Tissue and Bone Sarcoma Group. LeCesne A, Judson I, Crowther D, Rodenhuis S, Keizer HJ, Van Hoesel Q, Blay JY, Frisch J, Van Glabbeke M, Hermans C, Van Oosterom A, Tursz T, Verweij J.	
	Bone	IV	12 / 13				J Clin Oncol 1993 Jul;11(7):1276-85. An intergroup phase III randomized study of doxorubicin and dacarbazine with or without ifosfamide and mesna in advanced soft tissue and bone sarcomas. Antman K, Crowley J, Balcerzak SP, Rivkin SE, Weiss GR, Elias A, Natale RB, Cooper RM, Barlogie B, Trump DL, et al.	
Unknown Primary	Carcinoma	IV	11				Am J Clin Oncol 2001 Aug;24(4):372-5. Combination of cisplatin-doxorubicin-cyclophosphamide in adenocarcinoma of unknown primary site: a phase II trial. Guardiola E, Pivot X, Tchicknavorian X, Magne N, Otto J, Thyss A, Schneider M.	
		IV	8				Am J Clin Oncol 2000 Dec;23(6):614-6. Multicentric phase II study of cisplatin and etoposide in patients with metastatic carcinoma of unknown primary. Voog E, Merrouche Y, Trillet-Lenoir V, Lasset C, Peaud PY, Rebattu P, Negrier S.	
		IV	13				J Clin Oncol 1997 Jun;15(6):2385. Carcinoma of unknown primary site: treatment with 1-hour paclitaxel, carboplatin, and extended-schedule etoposide. Hainsworth JD, Erland JB, Kalman LA, Schreeder MT, Greco FA.	Single institution

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[1] Field MJ, Cassel CK, eds. *Approaching Death: Improving Care at the End of Life*. Washington, DC: National Academy Press; 1997:59-64. ISBN:0309063728. Full Text

[2] Hagerty RG, Butow PN, Ellis PM et al. Communicating with realism and hope: incurable cancer patients' views on the disclosure of prognosis. *J Clin Oncol.* 2005 Feb 20;23(6):1278-88. PMID: 15718326. Full Text

In a survey of terminally ill patients, 126 (58% response rate) reported the following: 98% said they wanted their oncologists to be realistic, provide an opportunity to ask questions, and acknowledge them as an individual when discussing prognosis. Doctor behaviors associated with hope were: up to date treatment (90%), appearing to know about the patient's cancer (87%) and saying pain will be controlled (87%). Behaviors not instilling hope were appearing nervous or uncomfortable (91%), giving prognosis to family first (87%) or using euphemisms (82%).

[3] Sekimoto M, Asai A, Ohnishi M, Nishigaki E, Fukui T, Shimbo T, Imanaka Y. Patients' preferences for involvement in treatment decision making in Japan. *BMC Fam Pract.* 2004 Mar 1;5(1):1. PMID: 15053839. Full Text.

[4] Jadalla A, Sharaya H. A Jordanian view about cancer knowledge and attitudes. *Cancer Nurs.* 1998 Aug;21(4):269-73. PMID: 9691509. Full Text.

An assessment of Jordanian knowledge and attitudes about cancer. 81.5% of the participants want to know their diagnosis if they have cancer.

[5] Christakis N, Lamont E. Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study. *BMJ.* 2000 Feb 19;320(7233):469-72. PMID: 10678857. Full Text

To describe doctors' prognostic accuracy in terminally ill patients and to evaluate the determinants of that accuracy. 343 doctors provided survival estimates for 468 terminally ill patients at the time of hospice referral. Doctors overestimated survival by a factor of 5.3. Few patient or doctor characteristics were associated with prognostic accuracy. Doctors in the upper quartile of practice experience were the most accurate. As duration of doctor-patient relationship increased and time since last contact decreased, prognostic accuracy decreased.

[6] Vignano A, Doran M, Bruera E, Suarez-Alzamor ME. The relative accuracy of the clinical estimation of the duration of life for patients with end of life cancer. *Cancer*. 1999;86:170-176. FullText

The authors prospectively evaluated the accuracy of clinical estimation of survival (CES) in an inception and population-based cohort of 233 cancer patients who were seen at the onset of their terminal phase. They systematically review the literature on CES in advanced or end-stage cancer patients. Treating physicians overestimate the duration of life of end of life ill cancer patients, particularly those patients who die early in the terminal phase and who may potentially benefit from earlier participation in palliative care programs.

[7] Glare P, Virik K, Jones M, et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. *BMJ*. 2003;327:195-200 Full Text

Cochrane Library, Medline (1996-2000), Embase, Current Contents, and Cancerlit databases as well as hand searching were utilized to systematically review the accuracy of physicians' clinical predictions of survival in terminally ill cancer patients. The authors conclude that although clinicians consistently overestimate survival, their predictions are highly correlated with actual survival.

[8] Justice AC, Covinsky KE, Berlin JA. Assessing the generalizability of prognostic information. *Ann Intern Med*. 1999;130:515. Full Text

This paper describes an approach for evaluating prognostic systems based on the accuracy (calibration and discrimination) and generalizability (reproducibility and transportability) of the system's predictions.

[9] Oxenham D, Cornbleet MA. Accuracy of prediction of survival by different professional groups in a hospice. *Palliat Med.* 1998;12:117-182.

Examines the accuracy of prediction of prognosis by different professional groups in hospice. Importance of length of patients survival; Necessity for health workers to make accurate predictions for probably short survival; Analysis on the predictions of patients.

[10] Johnstone PAS, Norton MS, Riffenburgh RH. Survival of patients with untreated breast cancer. *J Surg Oncol*. 2000;73:273-277. Full Text

This article analyzes historical survival data of >1000 patients with untreated breast cancer. Five and ten year survival rates were about 18% and 4%, respectively.

[11] Kowalski LP, Carvalho AL. Natural history of untreated head and neck cancer. *Eur J Cancer*. 2000;36:1032-1037. Full Text

This paper describes the characteristics and natural history of the largest reported group of patients with untreated head and neck cancer. The overall survival ranged from 1 day to 53.8 months (median 3.82 months). Performance status was the most significant predictor of survival. Approximately 50% of untreated head and neck cancer patients will die within 4 months of their diagnosis.

[12] Yates JW, Chalmer B, McKegney P. Evaluation of patients with advanced cancer using the Karnofsky performance status. *Cancer*. 1980;45:2220-2224.

An investigation of the reliability and validity of the Karnofsky Performance Status Scale (KPS) is presented. The authors conclude that the KPS has considerable validity as a global indicator of the functional status of patients with cancer.

[13] Mor V, Laliberte L, Morris JN, Wiemann M. The Karnofsky performance status scale: an examination of its reliability and validity in a research setting. *Cancer*. 1984;53:2002-2007.

The reliability and validity of the Karnofsky Performance Status Scale (KPS) as a measure of the functional status of cancer patients is reported. The KPS was found to be strongly related to two other independent measures of patient functioning. The relationship of the KPS to longevity in a population of terminal cancer patients documents its predictive validity.

[14] Maltoni M, Pirovano M, Scarpi E, et al. Prediction of survival of patients terminally ill with cancer. *Cancer*. 1995;75:2613-2622.

This prospective multicentric study to verify those clinical factors predictive of survival in 540 patients with terminal cancer. Multiple regression analysis revealed that only clinical prediction of survival, anorexia, dyspnea, palliative steroidal treatment, Karnofsky performance status, and hospitalization were independent predictors of survival.

[15] Evans C, McCarthy M. Prognostic uncertainty in terminal care: can the Karnofsky index help? *Lancet*. 1985;i:1204-1206.

Members of a terminal care support team recorded upper and lower estimates of prognosis based on KPS. Just over half of the actual survivals were within the estimate limits, and the estimates tended to be overoptimistic. For the initial observations on each patient, the Karnofsky index, gave a closer correlation with the actual survival than the estimates.

[16] Reuben DB, Mor V, Hiris J. Clinical symptoms and length of survival in patients with terminal cancer. *Arch Intern Med*. 1988;148:1586-1591.

Using data from the National Hospice Study, the correlation of 14 easily assessable clinical symptoms with survival in patients with terminal cancer was examined. Performance status was the most important clinical factor in estimating survival time, but five other symptoms had independent predictive value as well (shortness of breath, problems eating or anorexia, trouble swallowing, dry mouth, and weight loss).

[17] Loprinzi CL, Laurie JA, Wieand HS, et al. Prospective evaluation of prognostic variables from patient-completed questionnaires. *J Clin Oncol*. 1994;12:601-607.

A detailed questionnaire was administered to 1,115 patients with advanced colorectal or lung cancer. Data generated by the patient-completed questionnaire provided important prognostic information independent from that obtained by other physician-determined prognostic factors.

[18] Vigano A, Dorgan M, Buckingham J, et al. Survival prediction in terminal cancer patients: a systemic review of the medical literature. *Palliat Med*. 2000;14:363-374. Full Text

This paper evaluates the published medical literature concerned with the survival of patients with terminal cancer and identifies potential prognostic factors. On the basis of 24 studies, performance status, cognitive failure, weight loss, dysphagia, anorexia and dyspnoea appear to be independent survival predictors. Clinical estimation of survival by the treating physician appeared independently associated with survival but the magnitude of the association was small.

[19] Zubrod CG, Sheiderman MA, Frei E. Appraisal of methods for the study of chemotherapy in man: comparative therapeutic trial of nitrogen mustard and triethylene thiophosphoramide. *J Chron Dis*. 1960;11:7-33.

[20] Miller RJ. Predicting survival in the advanced cancer patient. *Henry Ford Hosp Med*. 1991;39:81-84. PMID: 1890012

This report presents available data for predicting survival for patients with advanced common concerns. The impact of performance status, sites and number of metastasis and response are considered.

[21] Bruera E, Miller MJ, Kuehn N, et al. Estimate of survival of patients admitted to a palliative care unit: a prospective study. *J Pain Symptom Manage*. 1992;7:82-86.

This is a prospective open study of 61 consecutive patients with advanced cancer admitted to a Palliative Care Unit who underwent survival estimation by two independent physicians after a complete medical exam. An independent research nurse also assessed each patient. The assessment included activity, pain, nausea, depression, anxiety, anorexia, dry mouth, dyspnea, dysphagia, weight loss, and cognitive status. Logistic regression showed a significant correlation between survival and dysphagia, cognitive failure, and weight loss. These three simple determinations can predict survival more or less than 4 wk as well as the assessments of two skilled physicians.

[22] Llobera J, Esteva M, Rifa J, et al. Terminal cancer: duration and prediction of survival time. *Eur J Cancer*. 2000;36:2036. Full Text

The objective of this study was to determine the duration of the terminal period, the prognostic ability of healthcare professionals to predict this terminal period and the factors that can improve the prognostic accuracy. In the final model, clinical prognosis (P=0.0094), asthenia (P=0.0257) and the Hebrew Rehabilitation Centre for Aged Quality of Life (HRCA-QL) Index (P=0.0002) were shown to be independent predictors of survival.

[23] Maltoni M, Nanni O, Pirovano M, et al. Successful validation of the palliative prognostic score in terminally ill cancer patients. *J Pain Symptom Manage*. 1999;17:240-247. Full Text

This work validates a previously constructed prognostic score for terminally ill cancer patients, the Palliative Prognostic Score (PaP Score).

[24] Pirovano M, Maltoni M, Nanni O, et al. A new palliative prognostic score: a first step for the staging of terminally ill cancer patients. *J Pain Symptom Manage*. 1999;17:231-239. Full Text

This study describes the construction of a simple prognostic score, the Palliative Prognostic Score, which includes the following variables: Clinical Prediction of Survival (CPS), Karnofsky Performance Status (KPS), anorexia, dyspnea, total white blood count (WBC) and lymphocyte percentage.

[25] Ralston SH, Gallacher SJ, Patel U, et al. Cancer-associated hypercalcemia: morbidity and mortality. clinical experience in 126 treatment patients. *Ann Intern Med*. 1990;112:499-504. Full Text

This retrospective study reviews the effects of antihypercalcemic treatment on morbidity and mortality in cancer-associated hypercalcemia.

[26] Gaspar L, Scott C, Rotman M, et al. Recursive partitioning analysis (RPA) of prognostic factors in three Radiation Therapy Oncology Group (RTOG) brain metastases trials. *Int J Radiat Oncol Biol Phys*. 1997;37:745-751. Full Text

This paper presents an analysis of tumor/patient characteristics and treatment variables in previous Radiation Therapy Oncology Group (RTOG) brain metastases studies, including 1200 patients to evaluate the benefit of new interventions. Three patient classes with significantly different prognoses were identified: Class 1: patients with KPS > or = 70, < 65 years of age with controlled primary and no extracranial metastases; Class 3: KPS < 70; Class 2- all others.

[27] Agboola O, Beniot B, Cross P, et al. Prognostic factors derived from recurrence partition analysis (RPA) of Radiation Therapy Oncology Group (RTOG) brain metastases trials applied to surgically resected and irradiated brain metastatic cases. *Int J Radiat Oncol Biol Phys*. 1998;42:155-159.

This retrospective review of 125 patients who underwent surgical resection and irradiation of tumors metastatic to brain was undertaken to identify prognostic factors for survival and to determine if the prognostic factors used in the recursive partition analysis (RPA) of brain metastases cases from Radiation Therapy Oncology Group (RTOG) studies is applicable to surgically resected and irradiated patients. The three classes of patients defined from RPA, had median survivals of 14.8, 9.9, and 6.0 months respectively (p=0.0002). Age of < 65 years, KPS of > or = 70, controlled primary disease, absence of extracranial metastases, complete surgical resection of the brain lesion(s) were found to be independent prognostic factors for survival; the total dose of radiation was not.

[28] Chernow B, Sahn SA. Carcinomatous involvement of the pleura. *Am J Med*. 1977;63:695-702. PMID: 930945

To better define the prevalence, presentation, primary sites and survival of patients with Carcinomatous involvement of the pleura, 96 cases of carcinoma of the pleura diagnosed by cytopathology or closed pleural biopsy are reviewed.

[29] Burrows CM, Mathews WC, Colt HG. Predicting survival in patients with recurrent symptomatic malignant pleural effusions: an assessment of the prognostic values of physiologic, morphologic, and quality of life measures of extent of disease. *Chest*. 2000;117:73-78. Full Text

To determine the prognostic value of pleural fluid pH, pleural fluid glucose, extent of pleural carcinomatosis (EPC) score, and Karnofsky Performance Scale (KPS) score in patients with recurrent symptomatic malignant pleural effusions, 85 consecutive patients with recurrent symptomatic malignant pleural effusions who were referred to the interventional pulmonary service for thoracoscopic pleurodesis were evaluated. The KPS score was the only statistically significant predictor variable.

[30] Werner-Wasik M, Scott C, Cox JD, et al. Recursive partitioning analysis of 1999 Radiation Therapy Oncology Group (RTOG) patients with locally-advanced non-small cell lung cancer (LA-NSCLC): identification of five groups with different survival. *Int J Radiat Oncol Biol Phys*. 2000;48:1475-1482. Full Text

This analysis of patients with locally-advanced non-small-cell lung cancer (LA-NSCLC) was undertaken to identify characteristics predictive of survival in a large cooperative group patient population, and to define subgroups of the population with differing outcomes. The authors concluded that cisplatinum-based CT improves survival over RT alone. The presence of a malignant pleural effusion is a major negative prognostic factor for survival.

[31] Buckman R. *How to Break Bad News: A Guide for Health Care Professionals.* Baltimore, MD: The Johns Hopkins University Press; 1992:65-97.

[32] Garg A, Buckman R, Kason Y. Teaching medical students how to break bad news. CMAJ. 1997 Apr 15;156(8):1159-64. PMID: 9141988. Full Text

This article describes a program for teaching medical students how to break bad news. An evaluation of the program by the participants over a 5 year period is presented.

[33] Baile WF, Buckman R, Lenzi R, Glober G, Beale EA, Kudelka AP. SPIKES—A six-step protocol for delivering bad news: application to the patient with cancer. *Oncologist*. 2000;5:302-311.

A protocol for disclosing unfavorable information-"breaking bad news"-to cancer patients about their illness is described.

[34] Quill TE, Arnold RM, Platt F. "I wish things were different": expressing wishes in response to loss, futility, and unrealistic hopes. *Ann Intern Med*. 2001;135:551-555. Full Text

[35] Clever SL, Tulsky JA. Dreaded conversations: moving beyond discomfort in patient-physician communication. *J Gen Intern Med*. 2002;17:884-885.

Suggests ways to solve the problem of inconvenience faced by physicians while communicating with patients. Situations arising the inconvenience; Recognition of patient's feelings by the physicians; Response to colleagues in inconvenient situations; Creation of systems for health care at institutional level.

[36] Roter DL, Larson S, Fischer GS, Arnold RM, Tulsky JA. Experts practice what they preach: a descriptive study of best and normative practices in end-of-life decisions. *Arch Intern Med*. 2000;160:3477-3485. Full Text

This is a nonexperimental, descriptive study of audiotaped discussions. SETTING: Outpatient primary care practices in the United States to explore best practices by describing what physicians who are considered expert in the area of end of-life bioethics or medical communication do when discussing advance directives with their patients. Expert physicians gave less information about treatment procedures and biomedical issues and asked fewer related questions but tended toward more psychosocial and lifestyle discussion and questions. Experts engaged in more partnership building with their patients.