

Our Foggy Crystal Ball The Heart and Brain of Prognostication

DEB HARROLD, MD
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Doc....how long do I
have?

Conflict of Interest

Presenter – Dr. Deb Harrold

Relationships with commercial interests: none

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Consulting Fees: none

Other: none

Objectives

- Discuss our roles in providing estimates of life expectancy
 - THE WHY, WHO, HOW
 - WHAT DOES THE PERSON ASKING REALLY WANT TO KNOW?
- Discuss our ability to prognosticate
- Discuss tools that may help us better prognosticate
- Discuss some “tricks of the trade” to help us better prognosticate
- Help us feel better about our role in providing prognostic information

- “How long do I have?”
- “I’m going to Mexico next week....is that alright?”
- “Should I go home tonight?”
- “Is Mr. Smith appropriate for LTC?”
- “Follow-up at my office in 3 wks.”
- Is this person appropriate for a residential hospice bed?

We are asked to prognosticate everyday.

- A prognosis is a prediction of possible future outcomes of a treatment or a disease course based on medical knowledge and experience. Because of the uncertainty of the future, and the complex dynamic system of the human body, prognostication can seem mysterious, unknowable and powerful. Through applying scientific method, medicine has and can make advancements in predicting medical outcomes, despite the formidable task.

- Glare, Sinclair; Journal of Palliative Medicine 2008

BUT NOBODY TAUGHT ME HOW!!!

LIMITED SKILL in PROGNOSTICATION
MAY

Have a NEGATIVE IMPACT on the
ABILITY to PROVIDE QUALITY END OF
LIFE CARE

Why Prognosticate?

- To make better decisions
 - Clinical decision making
 - Research decision making
 - Resource allocation decision making
 - Policy decision making
 - Goal setting – patient and family

It changes decisions

- Appropriate prognostic information is needed to make informed advance care planning decisions
- Murphy et al.
 - 41% pt >65 wanted CPR before learning the true probability of survival, only 22% wanted it after learning the true probability of CPR survival and only 5% wanted CPR if they had a chronic disease in which life expectancy was estimated at less than one year

Informed Consent

To ensure adequate informed consent for ongoing care, the following areas should be reviewed as appropriate:

- A thorough appraisal of the clinical situation (diagnosis, comorbidities, pathology);
- The various treatment options based on the clinical situation;
- The prognosis of the patient based on the possible treatments; and
- The preferences of informed patients or proxies.

Having the Prognosis Discussion

We don't do it enough!

Longitudinal study –in hospitalized cancer patients in whom death was believed to be imminent

- ◆ the possibility that death was NOT discussed
- ◆ 62% for MRP and 39% for any health care provider

Are we DASHING HOPE?

Prognosis Discussion Dashing of Hopes?

- Hope and realism can occur simultaneously
- Patients express a continued need for hope even when they know and accept that they have a very limited life expectancy
- Discussing prognosis will change the focus of the hope
- Realistic hopes exist at all stages of the cancer

Our FOGGY Crystal Ball

OUR ABILITY TO PROGNOSTICATE

Foreseeing

Accuracy?

Accuracy of estimated survival time (within 1wk +or-)

...In a terminally ill population (advanced cancer or at time of hospice admission)

- 25%
- 50%
- 75%
- >75%

Optimistic or Pessimistic?

A. We overestimate the survival time?

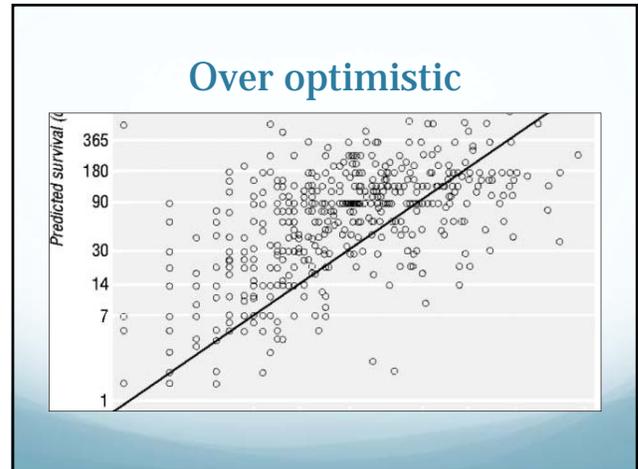
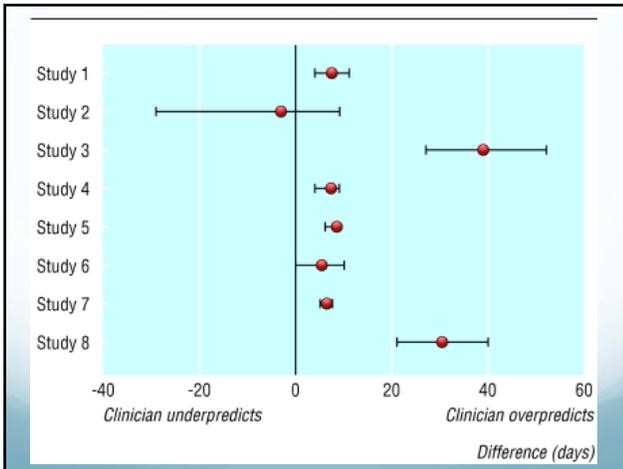
B. We underestimate the survival time?

ACCURACY

- The clinical prediction of survival was correct (within one week) in 25% of the cases
- BMJ 2003 – systemic review of 8 studies with over 1500 terminally ill cancer patients (advanced cancer – deemed terminal by authors or at time of hospice admission)

ACCURACY

- Only 20% of doctor's predictions were accurate (within 33% of actual survival); 63% were overoptimistic, 17% were overpessimistic
- BMJ 2000 – Prospective study of 468 terminally ill pts at the time of hospice admission



Optimism

- Overestimated >3/4 of the time when the clinical prediction of survival was 6 months or less
- Overestimated by at least 4 WEEKS in
 - 46% (BMJ 2000)
 - 27% (BMJ 2003)
- Underestimate by at least 4 WEEKS in
 - 13% (BMJ 2000)
 - 12% (BMJ 2003)

Accuracy?

Which scenario yields the most accurate diagnosis?

- A. Mrs. A. a 60yo woman with metastatic renal CA with a PPS of 30.
- B. Mr. B a 50yo man with pancreatic CA with a PPS of 60.
- C. Mr. C a 55yo man with metastatic colon CA with a PPS of 40.

Accuracy

- More accurate the sicker the patient is
 - PPS <40%

Table 2 R square values obtained for three multiple linear regression models in 981 patients for whom data on multiple prognostic variables were available

Model	KPS <40	KPS 40-50	KPS ≥60
CPS alone	0.46	0.35	0.24
Other prognostic factors alone	0.25	0.15	0.08
CPS and other prognostic factors	0.50	0.38	0.27

CPS=clinical prediction of survival; KPS=Karnofsky performance status score.

Education or Experience?

- Who would prognosticate better?
 - A. Oncologist that is MRP for patient
 - B. Oncologist that is not MRP for patient
 - C. Family Physician that is MRP for patient
 - D. Family Physician that is not MRP for patient

MRP, meaning pt is well known to them

To Know Them.....is to

- As the duration of the doctor patient relationship increased, so too did the doctor's odds of making an erroneous prediction
- Multivariate modeling showed that most types of doctors are prone to errors, in most types of patients
 - Doctors with oncology background are more accurate
 - The greater the experience of the physician the more accurate the prognosis

So, why bother counting on clinicians to prognosticate?

Clinical Predictions

- Physicians estimated survival time is inaccurate but is highly correlated with actual survival times
 - Log transformation of clinical prediction of survival was significantly correlated with the log transformation of the actual survival ($P < 0.001$)
- The systematic review in BMJ 2003
 - Found steroid use, anorexia, dyspnea, and the log of Karnofsky performance status score all contributed additional value to the clinical prediction of survival (CPS), but the added benefit was small

Foretelling....

Conversations on Prognostication

- How many of you believe that you would communicate a patient's predicted prognosis if asked by the patient or the patient's family?
- 23% of physicians would NOT communicate prognosis to their patients or patients' families if asked

Conversations on Prognostication

- How many of the people who would communicate the prognosis would communicate
 - an honest prognosis vs.
 - a discrepant prognosis?

Conversations on Prognostication

- 40% would communicate discrepant prognoses
- 37% would communicate honest prognoses
- Therefore almost ½ the time the clinician who is willing to communicate prognosis to their patients are communicating erroneous predictions.
- 70% of these are erroneously optimistic

Foreseeing..... and Foretelling....

- Both are VERY important
- Interesting study compared “formulated prognosis” vs. “communicated prognosis”
 - Median communicated survival = 90days
 - Median formulated survival = 75days
 - Median actual survival = 25days
 - Annals of Internal Medicine, 2001

Clinical Predictions of Survival

- Advantages
 - quick and cheap
 - Highly correlates with actual survival
 - Incorporates Advance Care Planning
- Disadvantages
 - Subject to biases (stronger MD-pt relationship)
 - Difficult conversation – could lead to erroneous predictions
 - Overestimates actual survival

Prognostic Tools

- No single tool is preferred
- Many tools incorporate CPS
- Newer models of prognostic tools utilize patient related prognostic factors
 - Performance Status
 - Comorbidities
 - Physiologic parameters

....SEE HANDOUT FOR SUMMARY OF AVAILABLE
PROGNOSTIC TOOLS

Next Steps

- “Would I be surprised if this patient died within the next 12 months?”
 - YES
 - NO
 - Discuss prognosis
 - Initiate advance care plan
 - Consider referral to hospice program and/or palliative care team

Tricks of “the TALK”

- Find out what they really want to know
 - “What to you know about.....?”
 - “What do you want to know about life expectancy?”
- “Pacing” the information giving may help achieve a balanced approach matching hope and realism
- Be honest- uncertainty can be an excellent starting place for discussion with patient

Tricks of “the TALK”

- Advance Care Planning ---work it in here!
 - The question how long have I got does show some acceptance of a deteriorating condition. This can be an opportunity to gently encourage saying and doing things that have been left unsaid and undone.
- Allow for Hope

Tricks of “the TALK”

- Avoid exact numbers, but also avoid euphemisms (poor, guarded...)
 - Days-wks, wks-months
 - “short”
- Watch the velocity of change
- Get a second opinion
- Actual survival is typically 30% shorter than predicted

Preparation is important

- Patients report that they want to have time to express their wishes, name decision makers, put financial affairs in order and make funeral preparations –they need prognosis information to best plan this
- Assess and reassess prognosis
 - Prognosis is not a one-time pronouncement. It is a time frame that will be adjusted and tightened over time
- Communicate to your patients

The Bottom Line

- Clinical prediction is important, although we all need to improve our skills
- If anything we overestimate survival
- There are lots of tools to help support your clinical prediction – PPS, internet
- Keep your eyes and ears open for opportunity to learn about prognosis and opportunity to discuss it with your patient!

The ‘X’ Factor

- Survival is somewhat tied to one’s will to live
- Each patient will have a different degree of a will to live or to die

Prognosticating length of survival is not without risks. With underestimation, families might believe they were robbed of time. Overestimation might cause excessively aggressive use of toxic treatments or a delay in referral to palliative care services.

Questions?

Cases

- Mr. B
 - COPD, anorexia, metastatic prostate CA
 - Admitted to hospice
- Mr. H
 - Neuroendocrine tumor unknown primary – brain mets
 - Decisions re:chemo/radiation
- Mrs. M.
 - 88yo previously very healthy; unconscious ?CVA
 - Decisions re:investigations

Prognostic Scales – Review

2006 European Society for Medical Oncology

- Palliative Prognostic Score (PaP)
 - most used
 - validated
 - cancer and non-cancer
 - good at predicting pts with poorest survival and less good at good and intermediate prognosis

Karnofsky performance status	
≥50	0
10-40	2.5
Clinician Prediction of Survival (weeks)	
>12	0
11-12	2
7-10	2.5
5-6	4.5
3-4	6
1-2	8.5
Total white blood cell count	
Normal (4800-8500) cell/mm ³	0
High (8501-11 000) cell/mm ³	0.5
Very high (>11 000) cell/mm ³	1.5
Lymphocyte percentage	

PaP Score

- Advantages
 - highly predictive of 30day survival
 - Combines clinical prediction with performance status and symptoms and lab parameters
- Disadvantages
 - Requires lab work
 - Prediction only up to 30days
 - KPS groupings?

Prognostic Scales – Review

2006 European Society for Medical Oncology

- Palliative performance index (PPI)
 - improvement when compared to clinical prediction alone

		Max. Possible
Palliative Performance Scale	10 – 20	4.0
	30 – 50	2.5
	> 60	0
Oral Intake	Severely Reduced (≤ mouthfuls)	2.5
	Moderately Reduced (> mouthfuls)	1.0
	Normal	0
Edema	Present	1.0
	Absent	0
Dyspnea at rest	Present	3.5
	Absent	0
Delirium	Present	4.0
	Absent	0
<i>Total</i>		15

Prognostic Scales – Review

2006 European Society for Medical Oncology

- Chuang prognostic score (CPS) – need more study
- Terminal Cancer Patient Score (TCP) –not validated

Palliative Performance Scale

- Studied initially in inpatient setting, cancer patients
- Appears to be a good predictor of mortality for patients in palliative care setting
 - Low PPS highly predictive of limited survival
 - Less accurate with prognosis >90days
 - ?debatable – 3 bands of survival predictions
 - A drop of PPS from 50-30% is significant but of much more urgent concern if it happens over a 2 day period as opposed to 4 months.

PALLIATIVE PERFORMANCE SCALE (PPS)

%	Ambulation	Activity and Evidence of Disease	Self-Care	Intake	Conscious Level
100	Full	Normal Activity No Evidence of Disease	Full	Normal	Full
90	Full	Normal Activity Some Evidence of Disease	Full	Normal	Full
80	Full	Normal Activity with Effort Some Evidence of Disease	Full	Normal or Reduced	Full
70	Reduced	Unable Normal Job / Work Some Evidence of Disease	Full	Normal or Reduced	Full
60	Reduced	Unable Hobby / House Work Significant Disease	Occasional Assistance Necessary	Normal or Reduced	Full or Confusion
50	Mainly Sit/Lie	Unable to Do Any Work Extensive Disease	Considerable Assistance Necessary	Normal or Reduced	Full or Confusion
40	Mainly in Bed	As Above	Mainly Assistance	Normal or Reduced	Full or Drowsy or Confusion
30	Totally Bed Bound	As Above	Total Care	Reduced	Full or Drowsy or Confusion
20	As Above	As Above	Total Care	Minimal Sips	Full or Drowsy or Confusion
10	As Above	As Above	Total Care	Mouth Care Only	Drowsy or Coma
0	Death	-	-	-	-

Anderson, Fern et al. (1996) Palliative Performance Scale (PPS) a new tool. *Journal of Palliative Care* 12(1), 5-11

PPS – 3 bands

- Morita et al. – median survivals
 - 10%-20% - median survival = 6 days
 - 30%-50% - median survival = 41 days
 - 60%-70% - median survival = 108 days
- 50% or less – only 10% would be expected to survive more than 6 months

Prognostat

- Google it–Victoria Palliative Research Network
- Based on research database
- Prediction is based on four variable (age, gender, diagnosis and PPS)
- Cancer diagnoses only

<http://web.his.uvic.ca/Research/NET/index.php>

Adjuvant

- Through <http://prognosis.pallimed.org>
- Breast cancer, lung cancer and colon cancer

Palliative Medicine Review: Prognostication

PAUL A. GLARE, M.B.B.S., F.R.A.C.P.¹ and CHRISTIAN T. SINCLAIR, M.D.²

ABSTRACT

Prognostication, along with diagnosis and treatment, is a traditional core clinical skill of the physician. Many patients and families receiving palliative care want information about life expectancy to help plan realistically for their futures. Although underappreciated, prognosis is, or at least should be, part of every clinical decision. Despite this crucial role, expertise in the art and science of prognostication diminished during the twentieth century, due largely to the ascendancy of accurate diagnostic tests and effective therapies. Consequently, “Doctor, how long do I have?” is a question most physicians find unprepared to answer effectively. As we focus on palliative care in the twenty-first century, prognostication will need to be restored as a core clinical proficiency. The discipline of palliative medicine can provide leadership in this direction. This paper begins by discussing a framework for understanding prognosis and how its different domains might be applied to all patients with life limiting illness, although the main focus of the paper is predicting survival in patients with cancer. Examples of prognostic tools are provided, although the subjective assessment of prognosis remains important in the terminally ill. Other issues addressed include: the importance of prognostication in terms of clinical decision-making, discharge planning, and care planning; the impact of prognosis on hospice referrals and patient/family satisfaction; and physicians’ willingness to prognosticate.

INTRODUCTION

PROGNOSTICATION IN MEDICINE is a misunderstood and underappreciated skill. It stands, along with diagnosis and therapeutics, as a way of demonstrating knowledge and mastery of a disease. Being able to identify a disease or illness and subsequently treat and cure the patient have become hallmarks of medicine in the last century as our technology and knowledge have advanced. With this increased ability to alter a course of disease, our profession has not kept pace with advancements in predicting the likely outcomes, especially when the outcomes are life or death. A PubMed search (July 2007) for the terms “diagnosis,” “therapy,” or “prognosis” demonstrates a biased re-

search agenda: 5.6 million articles for diagnosis, 4.9 million articles for therapy, and 0.6 million for prognosis. Formal medical education opportunities focusing on prognostication are scarce, yet being asked “Doctor, how long do I have?” is one of the most important and most intimidating questions asked of our profession.¹

All physicians call on forecasting skills in all aspects of medicine to select treatments, prioritize diagnoses, and educate patients and families. For example, the statement, “You have pneumonia, and you will start antibiotics and should be feeling better in a couple of days,” involves aspects of diagnostic, therapeutic, and prognostic skills. Yet with the prior statement, physicians are unlikely to identify use of prognostica-

¹Department of Palliative Care, Sydney Cancer Centre, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia.

²Kansas City Hospice & Palliative Care, Kansas City, Missouri.

tion. Although prognostication can involve more than life or death, predictions of life expectancy are what most physicians consider when they hear the words “prognosis” and “prognostication.”

Many patients and families want information about life expectancy,² so palliative care physicians need to be prepared to respond to this request. One of the key roles for palliative care services is to initiate discussions on prognosis and goals of care,³ which have often been neglected prior to the consultation.⁴ An audit of 325 consecutive referrals to a palliative care service in an American academic teaching hospital indicated discussions on prognosis and goals of care was the most common function performed by the service, occurring in almost 95% of cases.⁵

A prognosis is a prediction of possible future outcomes of a treatment or a disease course based on medical knowledge and experience.⁶ Because of the uncertainty of the future, and the complex dynamic system of the human body, prognostication can seem mysterious, unknowable and powerful. Through applying scientific method, medicine has and can make advancements in predicting medical outcomes, despite the formidable task. A century ago, it would have been thought impossible to predict the landfall of hurricanes or the approach of a blizzard, but meteorology has begun to understand and predict the near-future outcomes of the complex dynamic system of Earth’s climate.

To address various issues requiring physicians to utilize prognostic skills, Fries and Ehrlich define the “the 5D’s of prognostication”⁷:

1. Disease progression/recurrence
2. Death
3. Disability/discomfort
4. Drug toxicity
5. Dollars (costs of health care)

Using this framework, examples of some typical day-to-day prognostic questions for palliative care physicians are shown in Table 1. Doctors prognosticate whenever a medical treatment decision is made, but how explicitly the prognosis is discussed with others is variable. In trying to determine if a septic patient will survive a trip from the intensive care unit (ICU) to the computed tomography (CT) scanner, a physician may make the decision independently or collaborate with other clinicians or the family. In discussing hospice referral, a physician may discuss appropriateness directly with the patient and family based on an explicit prognosis of a few months. A prognosis can also be inferred by the patient or family when not openly discussed, such as noticing less

TABLE 1. TYPICAL PROGNOSTIC QUESTIONS ENCOUNTERED BY PALLIATIVE CARE PHYSICIANS IN THEIR DAY-TO-DAY PRACTICE, BASED ON THE 5Ds OF PROGNOSTICATION

What is the median survival of a patient with colon cancer who has liver metastases?
What future problems will this patient with advanced oropharyngeal cancer and dysphagia develop if I put in a gastrostomy tube?
Will this patient with a cord compression walk again?
What is the chance of a patient with metastatic cancer returning home after an in-hospital cardiac arrest?
How long will this opioid-induced nausea last?
Will it cost more to manage this patient’s pain according to the recommended guidelines?

lab draws or less consultants rounding in the context of a rapid decline.

There are two components to the act of prognostication: formulation (or “foreseeing”), the physician’s cognitive or objective estimate of the future course of the patient’s illness, and communication (or “foretelling”), the physician’s discussion of the prediction with others. This paper focuses on the impact and formulation of prognosis in patients with advanced cancer. Formulating prognosis in patients with other life-limiting illnesses is covered elsewhere in this series. There are many articles on “how to break bad news” that often includes the archetype of communicating an unfavorable prognosis, so this will not be reviewed in detail here.^{8–11} Despite the neglect of prognostic formulation in modern health care, there are some helpful tools and key points necessary for effective palliative care.

IMPACT OF PROGNOSTICATION ON PATIENT AND FAMILY AND HEALTH CARE SYSTEMS

An openly discussed prognosis has the potential to greatly alter the treatment plan for a patient. Patient-centered medical care depends on shared medical decision making among the patient, family and health care staff. To ensure adequate informed consent for ongoing care, the following areas should be reviewed as appropriate:

- A thorough appraisal of the clinical situation (diagnosis, comorbidities, pathology);
- The various treatment options based on the clinical situation;
- The prognosis of the patient based on the possible treatments; and
- The preferences of informed patients or proxies.

Without the inclusion of possible outcomes expected from a particular treatment course, informed consent and shared-decision making could be considered to be incomplete.

One of the most robust modern studies on the impact of prognostication was the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment (SUPPORT), in which prognostic information was explicitly provided to try to improve end-of-life care.¹² Using a computer-generated algorithm to prognosticate, SUPPORT demonstrated increased advanced directives discussions between patient and physician when the patient was given an objective estimate of prognosis for surviving 2 months of 40% or less. Other findings from SUPPORT included patients being less likely to desire cardiopulmonary resuscitation (CPR) if the patient felt the prognoses to be “poor.”¹³ Murphy et al.¹⁴ demonstrated that knowledge of CPR outcomes greatly decreased the likelihood of choosing CPR during an acute illness. After watching a video on depicting living with advanced dementia, patients without dementia were more likely to choose comfort care over life-prolonging treatments.¹⁵

Clarification of prognosis is vital to ensure patients make decisions based on likely outcomes as opposed to merely hopeful results. Multiple palliative care teams can attest to patients being optimistic in regards to prognosis in light of metastatic disease, or incurable treatment options. This optimism of prognostication as perceived by patients may lead to the requesting of medical technologies and treatments that would not be chosen if a more accurate and realistic prognosis was formulated and clearly communicated.

Palliative care teams frequently are able to realign goals of care based on prognostic information. Prognostication can impact the decisions that patients and families make about time shared together, estate management, funeral planning, and other practical issues. Prognosis is also important for families in determining how to respond to the patient’s palliative care needs, such as deciding how to care for the patient at home to urgently summoning a relative from out of town to visit a dying loved one. Parents of children with cancer who realize there is no hope of cure are also more likely to choose palliative care.¹⁶

Families’ dissatisfaction with communication around prognosis and other end of life issues has been well documented in studies such as SUPPORT.¹⁷ Interviews with family members of the recently deceased reveal the competing types of information families request, particularly when the patient is near death¹⁸:

- An internal tension between wanting realistic prognostic information and still allowing room for hope.
- Family ambivalence about how much information the family can cope with and understand.
- Family members want different sorts of information for themselves versus the patient.
- Families need guidance interpreting what physicians communicate.
- Families need assistance understanding the aims of treatment given the prognosis.
- Families feel overwhelmed and poorly prepared to make choices on behalf of the patient.

The palliative care physician needs to be aware of these concerns when discussing prognosis and other end of life issues with families. Reviewing prognostic information repeatedly on multiple occasions is likely to be necessary to ensure adequate understanding by families.

Discharge planning is a crucial function of palliative care consult services,^{3–5} with discharge plans being established for a majority of referrals.^{4,5} Predicting the outcome is one of many complex functions to be considered when developing a discharge plan in terminally ill patients, and often goes beyond “time-to-death” to include the other dimensions of prognosis. The typical palliative care consult, where decisions/goals are usually central will involve predicting:

- The time frame of death;
- The impact of disease modifying therapies, including toxicities; and
- The future disease course (including symptoms, function, family impact, and financial issues).

The palliative care physician needs to integrate these prognostic data points into a cohesive whole and then match this information with the various options for providing the care (home, nursing home, hospice facility, hospital) and the patient and family’s goals, priorities and expectations. Will the patient become weaker or stronger? More or less mobile? Will the patient develop problems many families may have difficulty with (e.g., bleeding, incontinence, seizures, confusion)? Predicting these outcomes can be as difficult as predicting death.

The underutilization of hospice services in the United States is well documented, with only approximately one third of deaths occurring in hospice and the typical time of referral being closer to 1 month than the eligible 6 months.¹⁹ Many studies have been undertaken to try to understand the barriers to hospice

referral and these have been identified at all levels: patient and family, health care provider, health care system.

Whether physicians' difficulty with formulating a prognosis of less than 6 months is a major barrier is uncertain. One survey of health maintenance organization (HMO) physicians in northern California identified difficulty prognosticating as the principal barrier to hospice referral.²⁰ However, studies demonstrate physicians' ability to accurately distinguish patients with cancer with a prognosis of less than 3 months²¹ or less than 6 months.¹² The problem of prognosis and hospice referral is more likely related to physicians' attitudes about how and when to communicate a poor prognosis and initiate hospice discussions rather than to poor prognostic skills.²²

Palliative care has been referred to as hospice care within the hospital setting and independent of expected survival.²³ In a prognostic study of palliative care referrals in an Australian teaching hospital, the median survival was only 1 month.²⁴ British data also indicate palliative care teams are underutilized in general hospital wards, where up to 25% of patients may be deemed "palliative."²⁵ A better medical understanding of prognosis may help identify patients who are eligible for palliative care services.

PHYSICIAN WILLINGNESS TO PROGNOSTICATE AND RELATED BARRIERS

There have been few surveys undertaken of palliative care physicians' views on prognosis,²⁶ although it is well recognized that hospital palliative care teams can play a major role in improving patient insight, including knowledge about their prognosis.²⁷ A survey of close to 700 American generalists and specialists in the late 1990s provided a foundation for understanding physicians' attitudes to prognostication.²⁸ Although prognostication was a frequent act (performed 100 times per year by the "typical" oncologist), nearly 60% of physicians surveyed felt poorly trained in the task of prognostication. Clinicians reported difficulty in formulating and communicating a prognosis. Reasons for the stressfulness of prognostication identified in the survey included feelings that patients want too much certainty and accuracy from the prediction. In addition to the perception of a high standard, the study demonstrated physicians were intimidated by being judged by patients and other clinicians if the prognosis was wrong—although not as badly as for getting

the diagnosis wrong. Physicians were found to avoid prognosticating, generally waiting to be asked rather than volunteering a prediction. Doctors described more reluctance to prognosticate when the clinical situation was atypical and the course seemed more uncertain than usual.

When prognosticating, almost all physicians surveyed said they would be optimistic. Moreover, two thirds also admitted if the patient were optimistic about the prognosis then the physician would generally reinforce an optimistic view. Finally, almost all the surveyed physicians said they would try to avoid being specific when giving a prediction. These attitudes and behaviors have been described as the "professional norms" of prognosis,²⁹ and are summarized in Table 2. Because clarifying the prognosis is one of the key functions of hospital palliative care teams, education and training of palliative care physicians needs to focus on overcoming these tendencies of avoidance and deception in the effort to provide a false hope.

The sociologic study of medical culture and the barriers to prognostication is incomplete, but key issues are beginning to emerge. The centrality of diagnostics and therapeutics in medical practice may divert most physicians' interest in, and attention to, prognosis.²⁹ The conditional nature of a formulated prognosis means, unlike the diagnosis, it needs to be reformulated at regular intervals. This dynamic nature of prognosis can help balance the inherent uncertainty, but if physicians are already reluctant to prognosticate one time, it may be difficult to convince many to prognosticate on more frequent basis. The lack of formal educational opportunities about prognosis in medical schools, journals, and textbooks also contributes to lack of self-confidence.^{8,30}

Physicians believe in a prognostic self-fulfilling prophecy, and this understandably makes them less willing to formulate, let alone communicate, unfavorable prognoses.²⁹ Oncology is beginning to identify the common conflict between giving an unfavorable prognosis and maintaining hope in patients with advanced cancer.³¹ While most patients can be redirected toward hoping in more realistic outcomes, such as a

TABLE 2. PROFESSIONAL NORMS
REGARDING PROGNOSTICATION

-
1. Do not make predictions
 2. Keep what predictions you do make to yourself
 3. Do not communicate predictions to patients unless asked
 4. Do not be specific
 5. Do not be extreme
 6. Be optimistic
-

death with well-controlled symptoms or refocusing on the person as an “individual” and not as a patient, some patients will not accept this. Clinical inertia allows an oncologist to accede to the patients’ wishes and offer more treatment.³² Prognosis can be perceived as more emotional than diagnosis and therapy, especially when associated with death, thereby further repelling physicians from approaching the topic. The pressures of modern clinical practice impact open prognostication. As it has been said “it almost always takes less time to explain the side effects and schedule of a new treatment than it does to discuss death and dying.”³¹

The disclosure of prognosis to terminally ill patients may be impeded by medico-legal issues. Given greater demands for patient involvement in medical decision-making, the disclosure of terminal prognosis is being seen as ethically justified because it upholds the principle of self-determination and enables patients to make treatment decisions consistent with their life goals.³³ Prognostication is also the foundation for any discussion regarding medical futility and therefore may be called into question in an ethics committee or a court of law.

In view of the “norms of prognostication,” discussions about prognosis at the end of life often do not take place, and when they do, they are limited in scope. A study of the medical record of 232 randomly selected hospitalized patients in Connecticut with inoperable cancer examined the presence and content of discussions about prognosis and advanced care planning efforts.³⁴ Discussions about prognosis were documented in the medical records of only 89 (38%) patients. Physicians and patients were both present during the discussion in 46 (52%) of these cases. Time until expected death was infrequently documented. At most, a physician may write a prognosis as “guarded,” “poor,” or “terminal,” as if the profession had mutually agreed upon objective definitions. These terms are quite subjective and unfortunately appear in research on prognostication as well, hampering efforts to accurately translate research from the journal to the bedside.

Even when prognosis is discussed, concerns remain about the openness of such discussions.^{35,36} Increasing evidence demonstrates doctors may be shifting from withholding to revealing a terminal prognosis in advanced industrial societies. However this revealing of a prognosis may use “partial and conditional” rather than “full and open” disclosure.³⁵ A collusion in physician–patient communication about imminent death may result in a “false optimism about recovery.”³⁶ This collusion is a result of physicians’ activism and pa-

tients’ adherence to the treatment calendar and the “recovery plot,” which allows both to avoid acknowledging explicitly what should and could be known. The physician may desire and refuse to communicate a poor prognosis, while the patient may desire and refuse to hear it, but neither is willing to take the first step. Patients gradually discover or realize the poor prognosis by various means, from witnessing their physical deterioration to contact with others who may be dying to reading the actions of others around them. Solving the problem of collusion between physician and patient requires an active, patient-oriented approach by the physician. Perhaps solutions can be found outside the physician–patient relationship itself, for example, involving “treatment brokers” for which palliative care physicians may possibly play a role.³⁷

DETERMINING PROGNOSIS IN ADVANCED AND TERMINAL CANCER

The approach to formulating an individual prognosis can be divided into two main methods. The clinician’s prediction of survival (CPS) depends on one’s clinical experience and knowledge to make a subjective judgment about an individual’s prognosis. The second method is actuarial estimation of survival (AES), which uses factors established through data and research to more narrowly define an individual prognosis for a patient.³⁸ AES typically involves indexes or scores which are then compared to a table defining various mortality data points. AES and CPS are not mutually exclusive, as a clinician may use a prognostic score or index as a starting point and refine the prognosis to the clinical scenario. Also, some prognostic indices use the CPS as part of the scoring system in addition to objective data.

The approach for both AES and CPS rely on many of the factors illustrated in Figure 1, adapted from MacKillop and colleagues. Many different data points may be called upon in AES and CPS depending on the clinical situation. Increasingly, tumor markers are identified as helpful determinants at time of diagnosis to help select therapy and predict possible response/outcome before clinical signs may suggest a prognosis. For prognostication closer to the time of death, functional status and simple prognostic indices are a growing area of research for application in the palliative care population (see Appendix A).

A common clinical roadblock to assisting patients and families with realistic prognostication is relying on statistics to communicate a general prognosis. Population-based median survivals (e.g., 6 months for

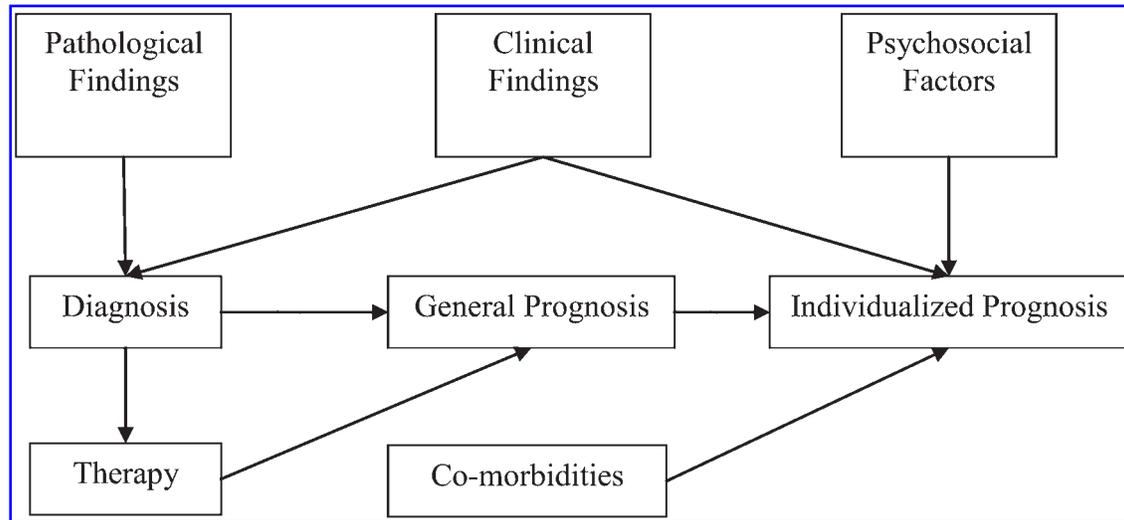


FIG. 1. Factors influencing an individual prognosis.

stage IV non-small-cell lung cancer) are available for many cancers. While this general prognosis guides the clinician on the outlook for the cancer and the impact of their treatments it may not be relevant to the individual and is not easily communicated. Also, median survival data often reflects the outlook at the time of diagnosis, not after treatment has been tried, so it is not very applicable to most palliative care patients in the midst of treatments. Historical survival analyses of untreated patients (either never treated or in “best supportive care only” arm of randomized trials) can be found for some cancer types but with new treatments repeatedly being discovered, it becomes difficult to compare a general prognosis from a study to the patient in front of you.^{39–44} Most importantly, “the median is not the message.” The survival curve in advanced cancer follows an approximately exponential function, so 80% of individuals will survive somewhere between one sixth and four times the median, the remaining 20% falling outside even this wide range.⁴⁵ Therefore the median has very little meaning for the individual patient.^{46,47} The physician’s goal is to formulate an individualized prognosis for the patient; starting with a generalized prognosis and modifying it, according to the patient’s using clinical observations, performance status, symptoms, comorbidities, will-to-live, and knowledge of illness trajectories.^{47,48}

The accuracy of survival predictions

Deciding whether to use CPS or AES or a combination should be determined by which is the most accurate but the comparison is not straightforward. There are two main types of survival predictions, temporal

(the patient will live a certain amount of time), expressed either as a continuous or categorical variable or probabilistic (the percentage chance of surviving to a certain time). Most studies of CPS have looked at temporal predictions where as most prognostic indexes (AES) provide probabilistic predictions. Not surprisingly, probabilistic predictions turn out to be more accurate than temporal ones. The accuracy of probabilistic predictions is on the order of 50%–75%^{21,49}; the accuracy of temporal predictions is poor, of the order of 25% (an accurate prediction being defined as the observed survival being $\pm 33\%$ of the predicted survival).⁵⁰ Few studies have compared probabilistic CPS and AES, and when they have, generally find only small differences in the accuracy of the two methods.^{12,51}

When analyzing prediction research, it is important to understand the terminology of measurement, including the terms discrimination, calibration, accuracy, and precision. Discrimination is the correct allocation of individuals from two or more discrete populations to the correct subpopulation without mismatch. Calibration is the adjustment of an instrument so the distribution of its measurements matches a standard.^{21,52} Accuracy measures the difference between all measured values (estimates) and the true value. This difference between the mean estimates for a population and the true survival allows us to discover if any optimistic or pessimistic biases exist. Precision defines how closely all estimates are to each other with repeated measurement. Tools can discriminate if probabilistic predictions are accurate and precise. Physicians are well calibrated if their temporal predictions are accurate and precise.

Clinician's prediction of survival

While actuarial judgment is generally preferred over subjective judgment in most areas of health care,³⁸ subjective judgments of survival remain relevant in palliative care, and are often retained as an independent survival predictor in multivariate analyses. A recent systematic review in patients with terminal cancer indicated CPS accounted for approximately half of the variance in observed survival, which was more than did the usual prognostic factors employed for AES (performance status, symptoms, abnormal laboratory tests).⁵³ The review also found a positive linear correlation between predicted survival and actual survival to 6 months but not beyond, thus confirming physicians' ability to discriminate between groups of terminally ill patients with cancer, according to their short-term survival. However, physicians are not well calibrated, as demonstrated by CPS being consistently inaccurate and biased in the overly optimistic direction—by as much as a factor of 3 to 5.⁵⁰ The experience and specialty of the physician and the nature of the physician–patient relationship may be confounders for the accuracy of the CPS.^{49,50}

A prospective study of CPS when making referrals to a U.S. hospice indicated academic oncologists were more accurate than community oncologists or family physicians and more experienced physicians were more accurate. However, this increased accuracy was blunted if the relationship between the physician and patient was strong. This led the authors to suggest an experienced but dispassionate specialist physician was likely to be the most accurate and might be requested for a prognostic 'second opinion' if an accurate prognosis was deemed essential (e.g., deciding to withdraw life sustaining treatment).⁵⁰

Despite its limitations, there are certain advantages to using CPS rather than AES, and palliative care clinicians should cultivate their prognostic skills. Some of these advantages include:

- The results of prognostic index studies may not be applicable to the patient.
- Requisite prognostic factors to calculate a prognostic index (e.g., recent laboratory test results) may not be available.
- Some prognostic tools require the CPS as an input.
- The index may not provide prognostic information in the format required for the clinical situation.

The European Association of Palliative Care's Working Group on Prognostication has recently recommended CPS is a valid means to obtain a general prognostic evaluation of patients but is subject to a se-

ries of factors limiting its accuracy. Its use is recommended together with other prognostic factors.⁵⁴

Actuarial estimation of survival

The main advantage of using actuarial judgment for prognostication over CPS is that multivariate analyses have isolated the most important factors which can be used to develop prognostic tools for clinical use. Multiple models and prognostic indices have been developed and applied in the past two decades in the quest for accurate prediction. Because of the lack of consistency amongst prognostic factors between cancer patients, and because of variation in the accuracy of physicians' judgments (CPS), no single prognostic index has been universally successful in predicting outcomes across patient populations. Some of the more widely recognized prognostic tools researched and statistically validated in various patient populations are described briefly in Appendix A. The authors recommend the reader to become familiar with any tool before applying it in clinical practice.

A key concept for palliative care physicians to appreciate when considering prognostic factors in advanced cancer is that tumor-related factors important in the earlier stages of the disease (e.g., primary tumor site, size, grade, extent of disease, marker levels, chromosomal abnormalities) are much less important than factors related to the individual with the disease.^{55,56} Some of the common patient-related factors in many prognostic indices include:

- Performance status (Karnofsky, Palliative Performance Scales);
- Signs and symptoms relating to nutritional status (e.g., anorexia, weight loss);
- Other key symptoms, particularly dyspnea and confusion (but not pain); and
- Some simple biologic parameters: serum albumin level, number of white blood cells and lymphocyte ratio.^{54,56–58}

A current limitation of applying actuarial judgment to palliative care prognoses is these factors only account for a small part (approximately one third) of the variance in observed survival, and novel prognostic factors are urgently needed.

CONCLUSION

While physicians have barriers to effective and frequent prognostication, it is a core clinical skill for the

palliative care physician to develop and maintain. Just as palliative care has influenced the mainstream health care system with its contributions to pain management and end of life care, it can also take a leadership role in making prognostication less difficult and stressful for others. While we should take a much broader view of prognostication, the main contribution we can make is in formulating (and communicating) survival predictions. While an increasing number of easy-to-use tools are becoming available to the clinician for this purpose, there is still a strong case for clinicians to cultivate subjective judgment skills. Developments in clinical epidemiology, biostatistical computing, and the conceptual basis of prognostication are leading to rapid developments in this area and palliative care physicians are at the forefront of this endeavor. More research needs to be done on all aspects of predicting death and other outcomes in palliative care.

Hippocrates wrote his *Book of Prognostics* more than 4000 years ago. Since then, medicine has only recently begun to reexamine this critical component of compassionate and scientific medical care. He closed his book with the following words, which are just as relevant today:

“he who would correctly identify beforehand those that will recover, and those that will die, and in what cases the disease will be protracted for many days, and in what cases for a shorter time, must be able to form a judgment . . . and reason correctly of them.”⁵⁹

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Address reprint requests to:

*Paul Glare, M.B.B.S.
Department of Palliative Care
Sydney Cancer Centre
Royal Prince Alfred Hospital
Missenden Road
Camperdown
NSW 2050
Australia*

E-mail: paul@email.cs.nsw.gov.au

APPENDIX A. PROGNOSTIC TOOLS

1. TOOLS FOR PATIENTS WITH AN ANTICIPATED SURVIVAL OF LESS THAN THREE MONTHS

1.1. National Hospice Study, United States, 1988

One of the earliest prognostic indices developed was generated from data collected from the cancer patients at the time of hospice enrollment for the National Hospice Organization (now the NHPCO) study in the 1980s.⁶⁰ The model combines performance state and symptoms to determine a probabilistic prognosis. These data showed the presence or absence of key symptoms in cancer patients with better functional status (Karnofsky Performance Scale [KPS]), to be divided into those with short or long prognoses. Of 14 symptoms studied 5 were predictive of a poor survival when the KPS score was greater than 50:

- Anorexia
- Weight loss
- Dysphagia
- Dry mouth
- Dyspnea

In patients with none of these symptoms, the median survival was 6 months; if all the symptoms were

present it was only 6 weeks. What keeps this old study relevant is the presentation of specific survival data easily accessed at the bedside (Table 3). For example, a patient with a KPS score of 30–40 and anorexia, weight loss and dry mouth is expected to have a median survival of 59 days and a 10% chance of still being alive in 258 days. The drawback is the predictions are based on hospice patients more than two decades ago, challenging the modern application. Although internally validated on the source data set, these predictions have never been externally validated. Nevertheless this easy-to-use tool is worth revisiting.

1.2. Palliative Performance Scale (PPS), Canada, 1999

Not developed as a prognostic index, the PPS (61) is a modification of the KPS⁶² which provides an observer-rated score of a patient's general health from 100 (normal) to 0 (dead) The PPS uses an objective, structured rating framework more suited to contemporary health service delivery (Fig. 2) than the historic KPS definitions from the 1950s. The PPS was intended to measure performance status, but has recently been found to have prognostic value. Several external val-

TABLE 3. NHO STUDY MEAN SURVIVAL 2 × 2 TABLE

<i>KPS Score</i>	<i>10–20</i>		<i>30–40</i>		<i>≥50</i>	
	<i>50% dead</i>	<i>90% dead</i>	<i>50% dead</i>	<i>90% dead</i>	<i>50% dead</i>	<i>90% dead</i>
No symptom	53	232	115	50	172	450
T	44	193	95	415	143	450
W	46	199	98	428	148	450
P	40	176	87	379	191	450
S	38	168	83	362	125	450
D	42	184	91	396	137	450
W, T	38	165	82	356	123	450
P, T	33	146	72	315	109	450
P, W	34	151	75	325	112	450
S, T	32	140	69	301	104	450
S, W	33	144	71	311	107	450
S, P	29	128	63	275	95	413
D, T	35	153	76	329	114	450
D, W	36	158	78	340	117	450
D, P	32	140	69	301	104	450
D, S	30	134	66	288	99	431
P, W, T	29	126	62	270	93	406
S, W, T	27	120	59	258	89	387
S, P, T	24	106	52	228	79	343
S, P, W	25	110	54	236	81	354
D, W, T	30	131	65	283	97	424
D, P, T	26	116	57	250	86	375
D, P, W	27	120	59	258	89	388
D, S, T	26	111	55	239	82	359
D, S, W	26	115	57	247	85	370
D, S, P	23	101	50	218	75	328
S, P, W, T	21	91	45	196	67	294
D, P, W, T	23	100	49	215	74	322
D, S, W, T	22	95	47	205	71	308
D, S, P, T	19	84	41	181	62	272
D, S, P, W	20	87	43	187	64	281
D, S, P, W, T	16	72	36	156	54	234

Median survival units are in days.

NHO, National Hospice Organization; KPS, Karnofsky Performance Scale; D, dry mouth; S, short of breath; P, problems eating/anorexia; W, weight loss; T, trouble swallowing/dysphagia.

Validation studies in various palliative care populations around the world are confirming the robustness and utility of the PPS, and much of this data has been recently reviewed.⁶³

Numerous studies have demonstrated a correlation between PPS scores and survival,^{64,65,66–68} although the median survivals for the different categories vary from study to study. Some authors claim the PPS is not highly discriminating between the some levels (e.g., 30% to 40% scores or 50% to 70% scores) and have argued for using the levels in “bands,”^{65,68} but a

multisite analysis of more than 1800 patients by the Victoria Hospice group has shown PPS levels are unique and a two-increment drop is highly significant (M. Downing, personal communication). The PPS has been shown to work well in nursing home and non-cancer populations.⁶⁷ PPS scores also correlate with symptom distress.⁶⁶

The original PPS was slightly modified in 2001 and the updated 2007 version can be downloaded from the Victoria Palliative Research Network website (<http://web.his.uvic.ca/research/NET/>).



**Palliative Performance Scale (PPSv2)
version 2**

PPS Level	Ambulation	Activity & Evidence of Disease	Self-Care	Intake	Conscious Level
100%	Full	Normal activity & work No evidence of disease	Full	Normal	Full
90%	Full	Normal activity & work Some evidence of disease	Full	Normal	Full
80%	Full	Normal activity <i>with</i> Effort Some evidence of disease	Full	Normal or reduced	Full
70%	Reduced	Unable Normal Job/Work Significant disease	Full	Normal or reduced	Full
60%	Reduced	Unable hobby/house work Significant disease	Occasional assistance necessary	Normal or reduced	Full or Confusion
50%	Mainly Sit/Lie	Unable to do any work Extensive disease	Considerable assistance required	Normal or reduced	Full or Confusion
40%	Mainly in Bed	Unable to do most activity Extensive disease	Mainly assistance	Normal or reduced	Full or Drowsy +/- Confusion
30%	Totally Bed Bound	Unable to do any activity Extensive disease	Total Care	Normal or reduced	Full or Drowsy +/- Confusion
20%	Totally Bed Bound	Unable to do any activity Extensive disease	Total Care	Minimal to sips	Full or Drowsy +/- Confusion
10%	Totally Bed Bound	Unable to do any activity Extensive disease	Total Care	Mouth care only	Full or Drowsy +/- Confusion
0%	Death	-	-	-	-

Used with permission Victoria Hospice Society, 2006

FIG. 2. Palliative Performance Scale (version 2).

**1.3. Palliative Prognostic Index (PPI),
Japan, 1999**

The Palliative Prognostic Index is an extension of the PPS, and uses four bedside parameters to predict a probabilistic short-term survival of terminally ill cancer patients (likelihood of being alive at 3- and 6-weeks; Table 4).⁶⁹ A total score of more than 6 predicts a survival of less than 3 weeks, a score of 5 or 6 predicts a survival of less than 6 weeks, a score of less than 5 predicts survival of more than 6 weeks.⁶⁹ The PPI was subsequently shown by the investigators to improve the accuracy of CPS when the PPI score was available to physicians, from 62% accurate without to 74% with.⁵¹ It has been used successfully by at least one other group in an unpublished study (C. Stone, personal communication). Limitations of the PPI include the challenge of accurately diagnosing delirium and its rather low negative predictive value (71%–87%).

**1.4. Palliative Prognostic (PaP) Score,
Italy, 1999**

The Palliative Prognostic (PaP) Score was constructed *de novo* by integrating the statistically signif-

icant results from multivariate analyses of 36 clinical parameters and biologic variables measured in 519 Italian hospice-home care patients (median survival 32 days).⁷⁰ The significant factors predictive of mortality retained in the model included:

- KPS score of 10 or 20
- Anorexia, dyspnea
- High total white blood count
- Low lymphocyte percentage
- CPS (in weeks)

Each of these five retained factors is given a subscore, based on its regression coefficient in the model. To calculate the PaP score for a patient, the subscores for each factor are summed, giving a total score ranging from 0 to 17.5 (Table 5). The PaP score categorizes patients into one of three probabilistic iso-prognostic groups with good (>70%), intermediate (30%–70%), or poor (< 30%) chance of surviving the next 30 days. The creators of the PaP score undertook a successful multicenter validation study in Italy.⁷¹ The robustness of the PaP score has been demonstrated by its validation in hospitalized patients with terminal cancer, advanced cancer, and various end-stage non-

TABLE 4. PALLIATIVE PROGNOSTIC INDEX (PPI)

Factor	Partial score
PPS 10–20	4
30–50	2.5
>50	0
Delirium	4
Dyspnea at rest	3.5
Oral intake: mouthfuls or less	2.5
Reduced, but more than mouthfuls	1
Edema	1

cancer illnesses.^{24,72,73} The original authors of the PaP score subsequently reported the median survival was shorter for each group in patients with delirium,⁷⁴ but they have not modified the PaP score to include a partial score for delirium.

1.5. Other Stratification-Based Predictive Models

Terminal Cancer Prognostic (TCP) Score, Korea, 2001

This study used data from just 91 patients with solid tumors no longer receiving anticancer therapy (median survival 54 days) to develop a prognostic model. Multivariate analysis adjusted for the primary tumor site demonstrated three were independent negative predictors of survival:

- Severe anorexia
- Severe diarrhea
- Mild confusion

The TCP score, based on three predictors, has been shown to be accurate for predicting survival.⁷⁵

Taiwanese Study, 2004

Unlike most other prognostic studies in terminal cancer, this recent work reported the metastatic site (liver, lung) is independently important as a prognostic factor, in addition to the usual type of factors:

- Performance status
- Symptoms (weight loss, tiredness, cognitive impairment)
- Simple clinical signs (edema, ascities).

These investigators used these factors to devise a scale ranging from 0 (no altered variables) to 8.5 (maximal alteration for all variables). A scores of more than

3.5 predicts a survival of less than 2 weeks, a score of more than 6 predicts survival of less than 1 week.⁷⁶

Intrahospital Cancer Mortality Risk Model, Turkey, 2004

This study aims to address the important practical issue of trying to determine which advanced cancer patients are likely to die during hospitalization in a metropolitan university teaching hospital.⁷⁷ The analysis of 13 retrospectively collected clinical and demographic variables found only 5 were significantly and independently predictive of a hospital death: poor performance status (ECOG performance status of 4), short duration of disease, emergency admission, low hemoglobin and high LDH. The proposed statistical model for the risk of dying in hospital was: $\log [\text{probability of death}/(1 - \text{probability of death})] = [5.53 + 4.89 \times \text{performance status (1 if ECOG} = 4, 0 \text{ if otherwise)}] - [\log \text{duration of disease (logarithmic transformation of duration in days)}] - [1.91 \times \text{type of admission (1 if elective admission, 0 if emergency admission)}] - [0.18 \times \text{Hb (g/dL)} + 2.27 \times \text{LDH (1 if} >378 \mu\text{mL, 0 if otherwise)}]$, and had an accuracy of greater than 80% for both the training set and testing set. It is yet to be validated elsewhere.

TABLE 5. HOW TO CALCULATE PALLIATIVE PROGNOSTIC SCORE⁷¹

Step 1: Allocate points for objective prognostic factors
Anorexia: 1.5 points
Dyspnea: 1 point
Karnofsky score 10–20: 2.5 points
Total white cell count
8.1–11.0 × 10 ⁻⁹ /L: 0.5 points
>11.0 × 10 ⁻⁹ /L: 1.5 points
Lymphocyte percentage:
12–20%: 1 point
12%: 2.5 points
Step 2: Formulate a subjective survival prediction in weeks
1–2 weeks: 8 points
3–4 weeks: 6.5 points
5–6 weeks: 4.5 points
7–10 weeks: 2.5 points
11–12 weeks: 2 points
>12 weeks: 0 points
Step 3: Sum points from step 1 and 2 to determine survival probability at 1 month
0.5–5 points: 1-month survival >70%
6–11 points: 1-month survival 30–70%
11.5–17.5 points: 1-month survival <30%

2. MORE THAN 3 MONTHS

2.1. SUPPORT Model, United States, 1995

Another early prognostic index was developed for use in the SUPPORT study.¹² While only one quarter of participants in this study had cancer and the study is only applicable to seriously ill hospitalized patients, it addresses some very important principles to further the science of prognostication. Furthermore cancer, as the primary disease or a comorbidity, was an important prognostic variable in the model. The SUPPORT Prognostic Model combines readily observable patient factors with a more complex physiology score similar to the APACHE III score to indicate the severity of disease. The final model included (in decreasing order of contribution):

- The physiology score.
- Glasgow Coma Scale score.
- Age.
- Disease class.
- Length of hospital stay.
- Cancer as comorbidity.

The physiology score is calculated by an extremely complicated mathematical formula given in the Appendix A of the article by Knaus et al.¹² utilizing 11 measures—disease type, vital signs, and biochemical parameters (including PaO₂)—recorded on day 3 of the hospitalization. The model used this information to generate individualized probabilities for surviving to 30, 60, 90, 120, 150, and 180 days. There were approximately 600 participants in SUPPORT with a primary diagnosis of lung cancer or metastatic colon cancer, and they had an overall median survival of 4–5 months. The model could predict which patients would be alive at 180 days with an accuracy of 78%. By comparison, the accuracy of their treating physicians' predictions of six months survival or not was 77%, more evidence physicians can discriminate when it comes to CES in advanced cancer. The authors interpreted this to show accurate objective estimates judgments such as the SUPPORT model provides can be generated and they can complement clinical judgment when making vital end-of-life decisions. Combining the physician judgment and the SUPPORT model's predictions increased accuracy slightly, to 82%. This landmark paper showed the potential for actuarial judgment in palliative care prognostication by producing high-quality objective individual survival predictions over a range of timeframes using large databases of prognostic factors and modern statistical

computing, even if not broadly applicable in its current format.

2.2. Survival Prediction Score (SPS), Canada, 2001

Canadian researchers initiated an analysis of survival for metastatic cancer patients at an outpatient palliative radiotherapy clinic in Toronto, Canada.⁷⁸ The final model contained five variables:

- Tumor details (primary, site of metastases)
- Performance status (KPS score)
- Three symptoms
 - Fatigue
 - Anorexia
 - Shortness of breath

Each variable is given a subscore and these are summed to produce the Survival Prediction Scores (SPS) ranging from 0 to 32. Patients were stratified by risk of mortality into three groups, with median survivals of approximately 12 months (for SPS ≤ 13), 4 months (SPS 14–19), and 2 months (SPS ≥ 20). This simple prognostic score needs external validation but can be useful and applicable to palliative care patients, especially those referred earlier in the course of their illness.

2.3. Good/Bad/Uncertain Index, United States, 1999

A stratification-based prognostic tool, the G/B/U Index was developed to build on the established Eastern Cooperative Oncology Group (ECOG) performance status measure by identifying a set of indicators to reflect the extent of disease and degree of suffering experienced by patients with advanced lung and bowel cancers.⁽⁷⁹⁾ The G/B/U Index is calculated from:

- Physician's assessment of performance status using ECOG score
- The physicians estimate of survival, compared to similar other patients
- Patient-rated performance (using KPS score)
- Patient-rated appetite

Criteria were set for positive, neutral, or negative implications for each variable. For example, an appetite rating of "increased" or "the same" had positive implications for the prognosis, "slightly reduced" was neutral, while "moderately reduced" or "markedly reduced" were considered to have negative prognostic

import. Patients were categorized as having a “good” prognosis if at least 3 of 4 variables were scored as “positive,” bad if a similar number were “negative” and the other patients were categorized as having an uncertain prognosis. Most patients in the study had ECOG scores of 0–1 and the median survival of the three groups was 15 months (good), 9 months (unsure) and 6 months (bad). It has not been externally validated.

2.4. Glasgow Prognosis Score, UK, 2005

The Glasgow Prognosis Score reflects the importance of inflammatory markers in disease progression, such as C-reactive protein (CRP) and a decrease in serum albumin. Recently, the simple process of scoring one point for each of hypoalbuminemia (serum albumin < 35 g/L) and elevated CRP (>10 mg/L) and simply adding the result for a combined score from 0–2 was prognostic in patients with advanced lung and gastrointestinal cancers.^{80,81} The median survival of the three groups (scores of 0, 1, and 2) was 17, 9, and 4 months respectively, in the case of the lung cancer patients. The advantage of this cumulative score, referred to by some as the Glasgow Prognosis Score (GPS), is that it is objective, relatively simple to measure, routinely available and well standardized. Its role in heterogeneous patients with cancer needs investigation.

2.5. CRP-Vitamin B₁₂ Product and Survival in Terminal Cancer

Vitamin B₁₂ is a blood test for which elevated levels have long been known to be associated with increased mortality in elderly patients with cancer⁸² and, more recently, other illnesses.⁸³ CRP (mg/L) and vitamin B₁₂ (pmol/L) have been combined as a prognostic index in terminal patients cancer, and the CRP*B₁₂ product was used to stratify a heterogeneous sample of advanced cancer patients into three iso-prognostic groups for risk of death at 3 months, based on whether the CRP*B₁₂ product was less than 10,000 (good), 10,000–40,000 (intermediate) or greater than 40,000 (bad).⁸⁴ These findings have subsequently been confirmed by another group.⁸⁵

3. MORE THAN THREE MONTHS: DISEASE-SPECIFIC TOOLS

A full discussion of this topic is beyond the scope of this paper. Interested readers are referred to the on-

cology literature, including the UICC textbook, *Prognostic Factors in Cancer (3rd edition)*.⁸⁶ Representative examples of tools for common cancers are given here only for completeness, with a particular emphasis on lung cancer on account of its commonality.

An important caveat is some of the models to be presented below are now more than 10 years old and often contain “cancer treatment” or “no cancer treatment” as a prognostic factor. Thus, they may no longer be valid given the changes in oncology practice. The traditional “cancer” death trajectory,⁴⁸ characterized by a stable period of reasonably good health followed by a fairly rapid decline to death over 1–2 months, may be changing as cancer becomes a chronic illness. There are, however, no data yet to support this supposition, but even it were the case, the lung cancer studies show performance status, symptoms, laboratory abnormalities and comorbidities continue to identify individuals with a worse outlook who may benefit from earlier access to palliative care.

3.1. Lung cancer

A prognostic index for predicting survival to 3 months in patients with inoperable non-small-cell lung cancer was developed in the early 1990s.⁸⁷ The four key factors in this index are: (1) extent of disease (extensive vs. limited), (2) poor performance status (ECOG 3–4), (3) weight loss (>10 pounds), and (4) lymphopenia (lymphocyte count $\leq 1 \times 10^9/L$). When each negative predictor scores one point, the likelihood of survival to 3 months is more than 95% for 0–1 points, 60%–75% for 2 points, and less than 20% for 3–4 points. When tested, the overall accuracy of prediction was 80%–90%, with 97%–99% specificity.

In the late 1990s a Finnish group obtained similar types of results, the five most powerful determinants of survival in inoperable lung cancer being disease extent, performance status, clinical symptom score, tumor size and hemoglobin level. These key prognostic variables of the index had equal impact on survival. Thus, based only on the number of adverse factors, the patient falls into one of the six possible prognostic groups. Ninety-eight patients (47%) with three or more risk factors had a 2-year survival rate of less than 2%, whereas 17 patients (8%) with no risk factor had a survival of 53% during a minimum follow up of 2 years.⁸⁸ A recent retrospective analysis of 112 patients with clinical stage III NSCLC enrolled in four radiation therapy oncology group studies at a single institution again showed a KPS ≤ 70 and comorbidities (severity index > 2 on Charlson score) were independently associated with inferior overall survival, whereas clinical tumor stage was not.⁸⁹

Recently, a French national study group has developed and validated a simple prognostic index for 4-year mortality in patients with NSCLC.⁹⁰ More than 4000 patients were enrolled with a median follow-up of 49 months. Five independent predictors of mortality were identified:

- Age (>70 years, 1 point);
- Gender (male, 1 point);
- Performance status at diagnosis (reduced activity, 3 points; active >50%, 5 points; inactive >50%, 8 points; and total incapacity, 10 points);
- Histologic type (large-cell carcinoma, 2 points);
- Tumor-node-metastasis (TNM) staging system (IIA or IIB, 3 points; IIIA or IIIB, 6 points; and IV, 8 points).

The minimum and maximum possible point scores were 0 and 22, respectively. Scores of the prognostic index were strongly associated with 4-year mortality: 0–1 points predicted a 35% (95% confidence interval [CI] 28–43) risk of dying within 4 years, 2–4 points a 59% (52–66) risk, 5–7 points a 77% (72–81) risk, 8–10 points an 88% (85–90) risk, 11–14 points a 97% (96–98) risk, and 15–22 points a 99% (97–100) risk. The survival curves for each group are given, so odds of surviving other periods can be read off.

3.2. Breast cancer

A prognostic index incorporating key prognostic factors was developed and validated in Japanese patients with metastatic breast cancer in the late 1990s.⁹¹ The prognostic factors in the index are: (1) history of adjuvant chemotherapy (ADJCT), (2) presence of distant lymph nodes (DLNs) and/or liver (HEP) metastases, (3) elevation of serum lactate dehydrogenase (LDH) and (4) short disease-free interval (DFI). The prognostic index is calculated by summing the sub-scores, as follows:

- ADJCT (not received = 0, received = 1)
- DLNs (absent = 0, present = 1)
- HEP (absent = 0, present = 1)
- LDH (< or = one times normal = 0, > one times normal = 1)
- DFI (> or = 24 months = 0, < 24 months = 2).

With this prognostic index, patients could be stratified into three risk groups. The median survival times of low-, intermediate-, and high-risk groups were 4 years, 2 years, and less than 1 year, respectively.

3.3. Colon cancer

Prognostic factors for survival of patients presenting with metastatic colorectal carcinoma (CRC) have recently been determined in a German study.⁹² In asymptomatic patients not needing surgery, just three of 13 factors investigated proved to be independent predictors of survival: performance status, CEA level, and chemotherapy. In patients with symptomatic primary tumors requiring palliative resection, three additional factors are significant: ASA-class, metastatic load, and extent of primary tumor. This paper is not very useful clinically, however, as it gives the hazard ratios for each factor, but is not in the form of an index/tool and does not give temporal or probabilistic prognoses.

3.4. Prostate cancer

A nomogram has been developed to make it easy for physicians to predict median, 1-year, and 2-year survivals for individual patients with hormone refractory metastatic prostate cancer, specifically prior to receiving chemotherapy.⁹³ The nomogram utilizes age, KPS, hemoglobin, prostate-specific antigen, lactate dehydrogenase, alkaline phosphatase and albumin. When validated on a heterogeneous patient sample (overall median survival of approximately 18 months, range 1 month to 7 years), the nomogram had an accuracy of 67%.

4. WEB BASED PROGNOSTIC TOOLS

4.1. Prognostigram

This tool is an interactive multimedia patient-specific prognostic tool for adult cancer patients, under development at the Washington University School of Medicine (St. Louis, MO) since 1999. It creates individualized survival curves based on data from the hospital-based tumor registry at Barnes-Jewish Hospital (St. Louis, MO) and the population-based SEER Program (National Cancer Institute, Bethesda, MD). Adjusted survival curves are generated, taking into account the impact of comorbid health information, and are presented on the same graphical figure as the survival curve for age, gender, and race-matched peers. Life survival curves are generated for patients at the time of diagnosis and for patients who have survived any number of years after diagnosis. Patient-unique survival curves generated by the Prognostigram program are displayed in a most straightforward format and are intended for patients, families, health care providers, and other professionals. Overlaid onto the survival curves is a second plot,

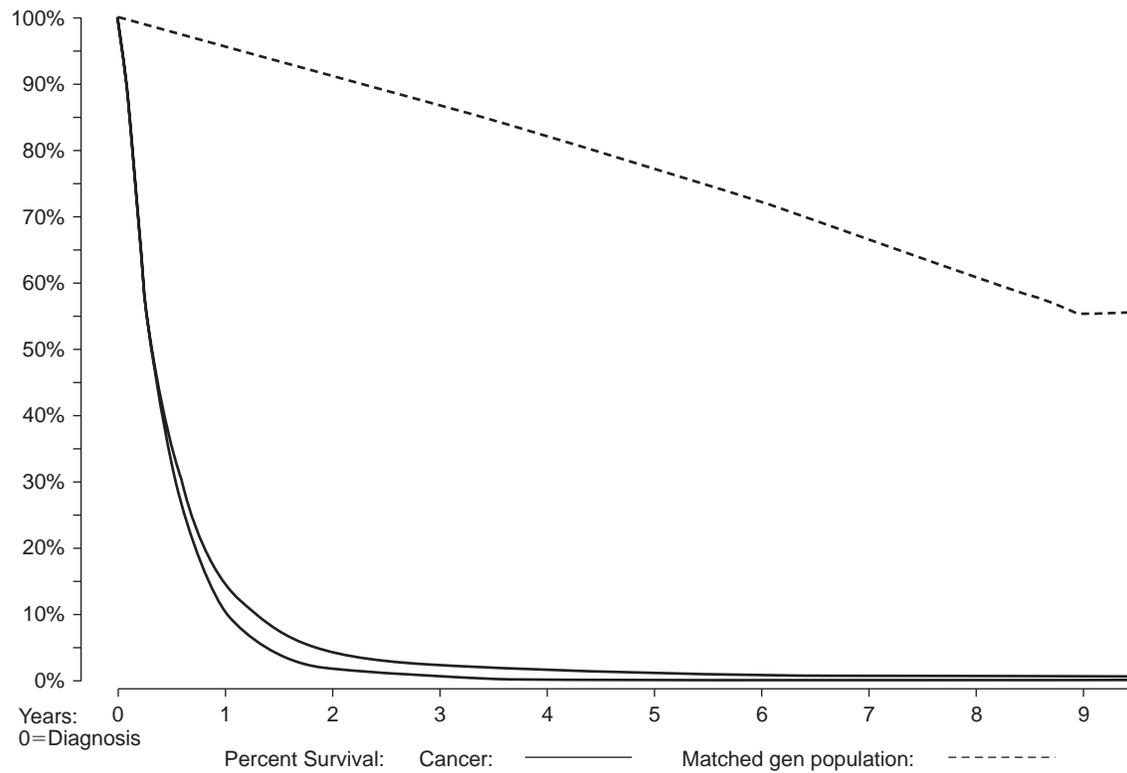


FIG. 3. Prognostigram Screenshot. White male, age 70–74, with newly diagnosed stage IV lung cancer, with and without comorbidities, and matched control (broken line).

Prognostat Criteria

Gender: Male

Age: 65 to 74

Diagnosis: Lung Cancer

PPS: PPS 60%

Submit Reset

Prognostat Results

	Survival Rate (%) in Days											No. of Patients
	1	2	4	7	14	30	45	60	90	120	180	
PPS 60%	100%	100%	100%	100%	88%	56%	38%	31%	25%	12%	6%	16
PPS 50%	100%	95%	87%	63%	39%	26%	24%	16%	13%	3%	3%	38
PPS 40%	100%	90%	73%	60%	38%	24%	11%	10%	3%	2%	2%	63
PPS 30%	97%	74%	56%	28%	15%	8%	5%	5%	0%	0%	0%	39
PPS 20%	91%	36%	23%	9%	5%	5%	0%	0%	0%	0%	0%	22
PPS 10%	42%	12%	0%	0%	0%	0%	0%	0%	0%	0%	0%	26
Overall PPS	91%	73%	60%	45%	29%	19%	12%	9%	5%	2%	1%	204

FIG. 4. Prognostat Screenshot. Predictions for palliative care patient, 70-year-old male with lung cancer.

demonstrating the natural mortality of a cohort of age-, gender-, and race-matched peers without cancer. Figure 3 shows the Prognostigram survival curve generated for a white male aged 70 to 74 years with metastatic lung cancer, with (purple line) and without (blue line) an adjustment for the prognostic impact of severe comorbidity. The 1-year survival rate goes from 15% to 10% and 2-year survival goes from 4% to 2%, respectively, on the comorbidity-adjusted curve—in each case a 50% reduction. The Prognostigram Web address is <http://oto.wustl.edu/clinepi/prog.html>, but is currently offline and out of use while version 2 is developed.

4.2. Prognostat

Prognostat is an interactive Web-based prognostic tool launched this year to estimate the chance and

duration of survival for a palliative care patient based on a small set of variables (gender, age, diagnosis, and initial PPS score). It is being developed by the Victoria Palliative Research Network in British Columbia, Canada. The survival estimates are derived from a research database of 5893 palliative care patients collected at the Victoria Hospice since 1994. Prognostat makes individualized probabilistic predictions expressed as the chance of being alive in a certain number of days. For example, a male aged 65–74 with lung cancer and a PPS of 60 at the time of referral to palliative care has a 56% chance of surviving 30 days and a 6% chance of surviving 180 days (Fig. 4). The Prognostat is currently accessible (accessed on July 9, 2007) and the Web address is: <http://web.his.uvic.ca/research/NET/tools/PrognosticTools/index.php>

Adjuvant! Online
Decision making tools for health care professionals

Adjuvant! for Lung Cancer (NSCLC)

Patient Information

Age:

Sex:

Comorbidity:

Pathological T and N as determined by definitive surgery leaving no known residual disease.

T of Primary Tumor:

N of Primary Tumor:

Stage:

Histologic Grade:

Tumor Diameter:

5 Year Risk:

Treatment Efficacy

Chem:

Proportional Risk Reduction (%):

Suppress treatment info dialogs

Results Graphs

Without Adjuvant Chemotherapy:

15.7 alive in 5 years.

79.5 die of cancer.

8.4 die of other causes.

With Adjuvant Chemotherapy:

15.7 alive in 5 years. Plus...

0.0 alive due to therapy.

79.5 die of cancer.

8.4 die of other causes.

Print Results PDF Access Help and Clinical Evidence

Clinical Trials Images for Consultations

© 2006 Adjuvant! Inc.

FIG. 5. Adjuvant! Online Screenshot.

4.3. Adjuvant! Online for Lung, Breast, and Colon Cancer

Adjuvant! Online is a Web-based tool for clinicians to discuss treatment options in regard to breast, lung and colon. Since the prognostic horizon is 10 years for this tool, it is obviously aimed at the oncologist, although some palliative care clinicians may find this to be a helpful tool to understand adjuvant treatment options. The tool is easy to use after a simple registra-

tion, and provides very useful graphs demonstrating possible survivals depending on course of treatment chosen (Fig. 5). The site has extensive information about how the prognostic estimates were developed, mostly based on SEER databases. A drawback is support by a pharmaceutical company, so transparency may be an issue, although the extensive documentation on the site makes this less of an issue. The Web address is: (<http://www.adjuvantonline.com/index.jsp>) (accessed July 9, 2007).

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