

Prognostication in advanced cancer

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THE ART OF ONCOLOGY: WHEN THE TUMOR IS NOT THE TARGET

Doc, How Much Time Do I Have?

By Charles L. Loprinzi, Mary E. Johnson, and Gretchen Steer

J Clin Oncol 2000;18:699

Mary Smith

- 42 female, married, 2 children, PH negative
- Recent Dx metastatic pancreatic cancer
- Had standard chemotherapy for 6 weeks
- CT shows progressive disease
- jaundiced; pain; getting weaker
- Oncologist: stop chemo, palliative care referral
- She asks you:

“How much time do I have?”

Quiz 1

How much time do you think she has?

1. Less than 2 weeks
2. One month
3. Six weeks
4. 3 months
5. More than 3 months

- *42F, married, 2 children*
- *Previously well*
- *Recent pancreatic ca*
- *Mets in liver*
- *POD on chemo*
- *pain; fatigue; poor PS*
- *Liver failure*
- *Oncologist: stop chemo, palliative care referral*

Quiz 2.

How will you answer her?

- Tell her the “truth”
- Give a more hopeful time frame
- Give a more negative time frame
- Say “No one knows”
- Avoid answering her question altogether

Answers

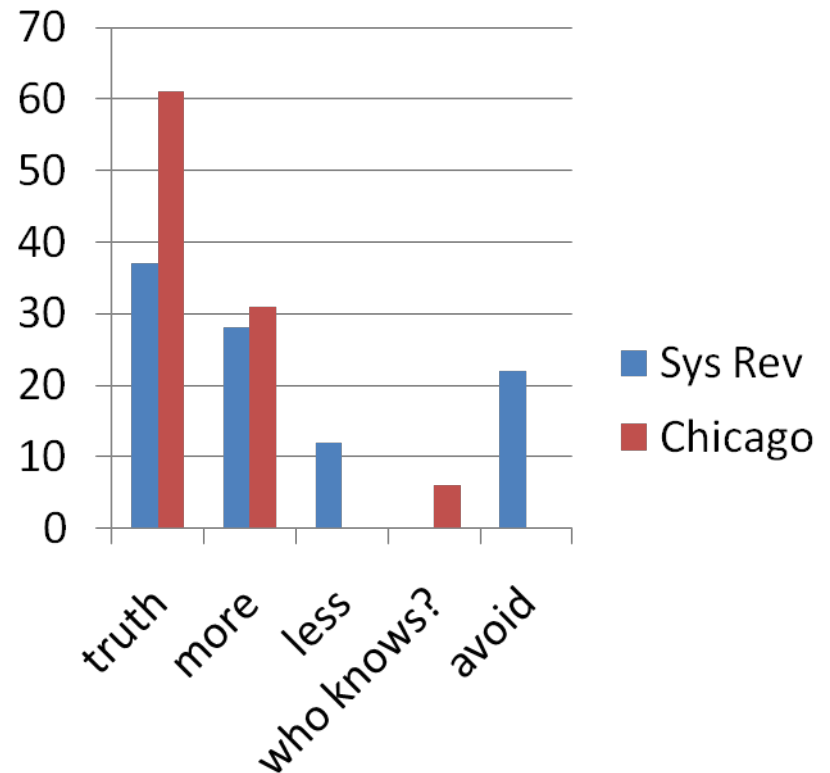
Quiz question 1: prediction

JCO (2001): **1 month**

Vancouver/Melbourne

- 20% did not answer
- 60% single number
 - **Median 2 months**
 - IQR 1-3 months
 - >6 months 15%
- 20% a range

Quiz question 2: prognosis



I want to die at home, Paul Newman tells his family as he's given 'weeks to live'

By [Andy Dolan](#)

Last updated at 6:43 PM on 08th August 2008 (died 9/27)



Frail: Paul Newman is wheeled out of hospital

U. S. physicians' experiences and attitudes to predicting survival

National random sample of 1311 internists

53% RR

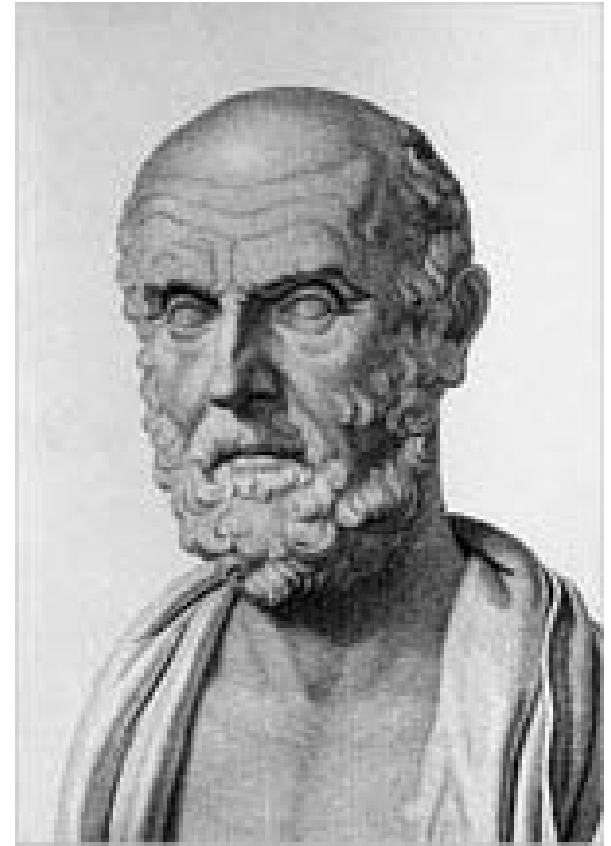
- Poorly trained
- Don't like doing it: stressful/difficult
- patients expect too much certainty

Christakis Arch Intern Med
1998;158(21):2389

Modern medical education in prognosis

Hippocrates' *Book of Prognostics*

It appears to me a most excellent thing for physicians to cultivate Prognosis; for by foreseeing and foretelling, in the presence of the sick, the present, the past and the future and explaining the omissions which patients have been guilty of, he will be the more readily believed to be acquainted with the circumstances of the sick; so that men will have the confidence to entrust themselves to such a physician”



The three great modern clinical skills

- Diagnosis
- Prognostication
- Therapeutics

Hutchinson, Lancet 1934

Why has prognosis gone out of vogue?

- Unscientific
- Unimportant
- unknowable
- inaccurate
- Unethical
- unprofessional



“A day in the life of Oscar the cat”

NEJM 2007; **Volume 357:328-329 (July 26)**

UNIMPORTANT: *therapy* replaces *prognosis* as the primary clinical act accompanying *diagnosis*



Pergamon

S0277-9536(96)00100-1

Soc. Sci. Med. Vol. 44, No. 3, pp. 301–315, 1997

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0277-9536/97 \$17.00 + 0.00

THE ELLIPSIS OF PROGNOSIS IN MODERN MEDICAL THOUGHT

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Abstract—Contemporary textbooks of internal medicine give scant attention to the prognosis of diseases. Has this always been the case? If not, when and why did prognosis come to be de-emphasized? Using a highly regarded, standard medical textbook initially authored by William Osler, *The Principles and Practice of Medicine*, I performed qualitative and quantitative content analysis of entries regarding lobar pneumonia in selected editions published between 1892 and 1988, with special attention to the period between 1892 and 1947. I chose lobar pneumonia because it was a leading cause of death throughout this period and because it is recognizable across time, thus making it possible to follow the evolution in clinical thinking about prognosis while holding constant the diagnosis. I argue that two powerful forces converged to lead to the ellipsis of prognosis: (1) the emergence of effective therapy, and (2) a fundamental change in the cognitive basis of medicine. With respect to the former, I show that there is a complementary, inverse relationship between the clinical acts of prognostication and

Pneumonia: Osler's textbook

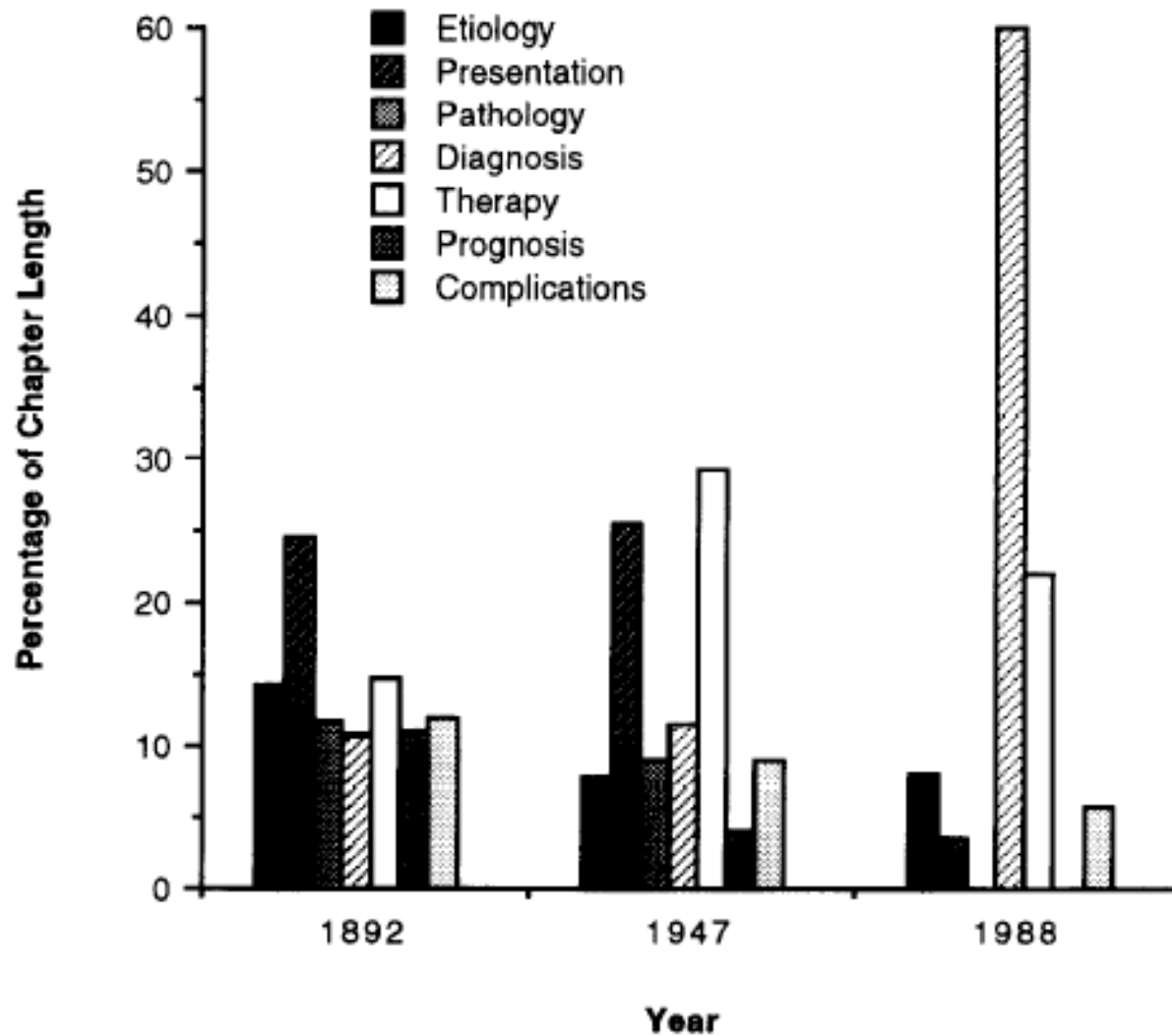



Fig. 1. Proportion of chapter length devoted to seven clinical tasks in 1892, 1947, and 1988

unknowable



“...For no-one knows the hour of his death except the Father” (Mark 13:32-7)

Inaccurate

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[< Hurricane Forecasters Embrace Uncertain\[...\] -- PREVIOUS](#) | [SEE ALL POSTS FROM THIS BLOG](#) | [NEXT](#)

June 5, 2008, 10:12 pm

When Dying Patients Are Given a Wrong Number

News reports openly speculating about Sen. Edward Kennedy's life expectancy after his brain-cancer diagnosis obscured a surprising truth about medicine: It doesn't do a good job of estimating how many days dying patients have left. My [print column](#) this week points out that life-expectancy stats aren't easily applied to individual patients, because age and other factors, some unknown, can make anyone an outlier.

The process of translating statistics into predictions for any one patient is further complicated by the human aspect of medicine. Patients and doctors often are reluctant to have the conversation about the number of days of life remaining. When they do, doctors tend to overestimate, perhaps out of self-confidence or of a wish to give hope to patients. And patients often don't absorb what they hear at this crucial moment, as demonstrated by a [Duke University study](#) of heart-failure patients this week.



Doctors' and patients' false optimism may be prompted in part by the irresistible stories of the [patients who beat the odds](#) — like the man this week who reportedly [won a bet](#) that he would outlive his doctors' predictions after he was diagnosed with mesothelioma.

At the University of California, Los Angeles, neuro-oncologists are [sharing data](#) on their patients' outcomes. It's an admirable approach, and one which could help give doctors and patients more realistic expectations, if more medical centers compiled and shared such data. But accurate prognosis for a specific patient will remain a challenge, particularly since doctors get much more training in diagnosis than in prognosis, [according](#) to Harvard's Nicholas A. Christakis, who has studied prognosis error.

Unethical

| | | | | | |
|-----------|----------|---------------|-------|--------------|--------------|
| HOME PAGE | MY TIMES | TODAY'S PAPER | VIDEO | MOST POPULAR | TIMES TOPICS |
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The New York Times
Wednesday, October 29, 2008

Health

| | | | | | | | | |
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RESEARCH FITNESS & NUTRITION MONEY & POLICY V

Well



Tara Parker-Pope on Health

October 22, 2007, 3:25 PM

When Doctors Steal Hope

A 79-year-old woman I know suffered a stroke recently, and a doctor in the emergency room told her family there was nothing he could do. The family was devastated. The woman's 24-year-old granddaughter ran to the parking lot and vomited, then spent the rest of the night at home with the family, sobbing with grief.

But the next day family members returned to the hospital room to see the woman sitting up, drinking a milkshake. The nurses even had her out of bed and walking to regain her strength. She clearly has a long recovery ahead of her, but three days after the doctor's first grim prognosis she left the hospital for a rehabilitation facility. The family was whipsawed by the emotional

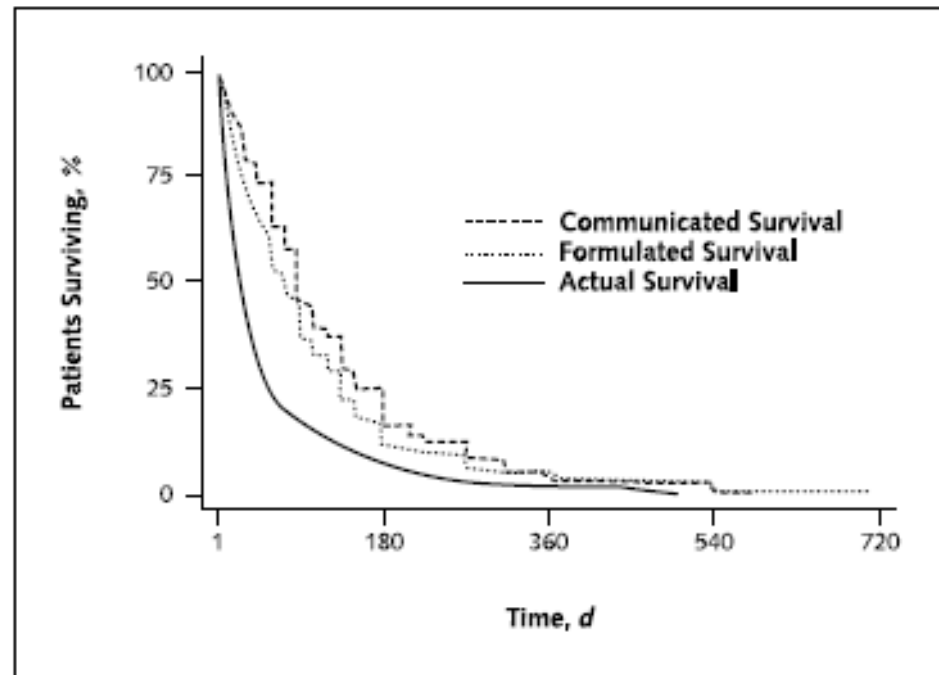
UNTRAINED

-> Physicians' norms of prognostication

- Avoid if possible
- Don't disclose it unless asked
 - Be vague
 - Don't be extreme
 - Be optimistic
- Don't share with colleagues

....also not very good at it

Figure 2. Relationship between communicated, formulated, and actual survival.



The differences between actual survival, formulated survival, and communicated survival in 300 terminally ill patients with cancer are shown. The median actual survival was 26 days, the median formulated survival was 75 days, and the median communicated survival was 90 days.

Wiley-Blackwell
Clinical Oncology

Prognostic Factors in Cancer

Third Edition

Edited by
Mary R. Gosselin
Brian O'Rourke
Leslie H. Sobin



Prognosis in Advanced Cancer

EDITED BY PAUL GLARE | NICHOLAS CHRISTAKIS



2. New concepts in prognosis

a. Two aspects of prognostication



1. Making the prediction
(foreseeing)
2. Communicating to the
patient
(foretelling)

2b. Prognosis & clinical epidemiology - more than predicting survival

- *the relative probabilities that a patient will develop each of the alternative outcomes of the natural history of his disease*

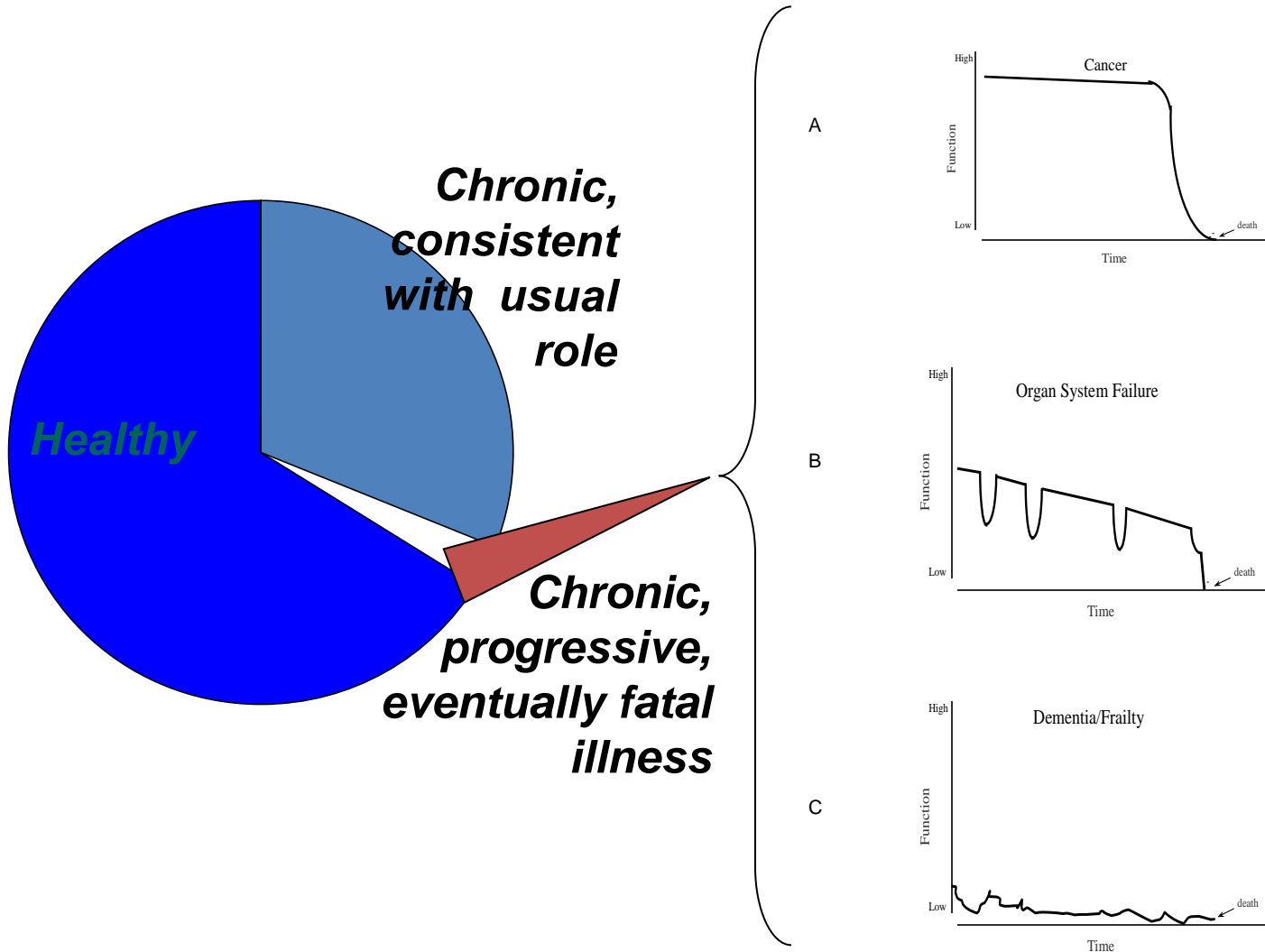
Sackett, 1991

“5D’s of prognosis”

- Death
- Disease progression/recurrence
- Disability/discomfort
- Drug toxicity
- Dollars (cost)

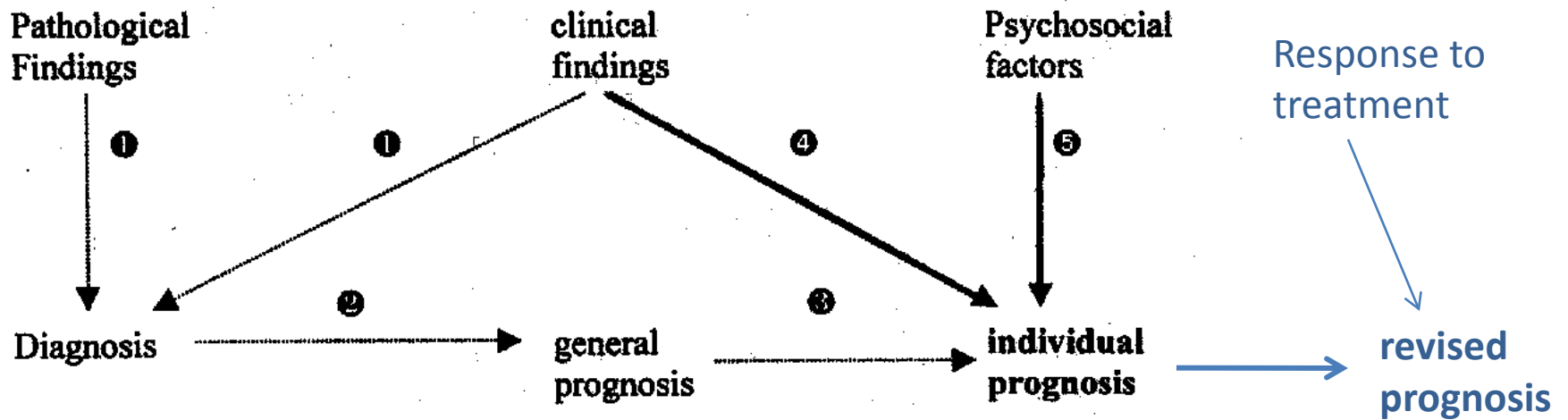
Fries & Ehrlich, 1980

2c. illness trajectories

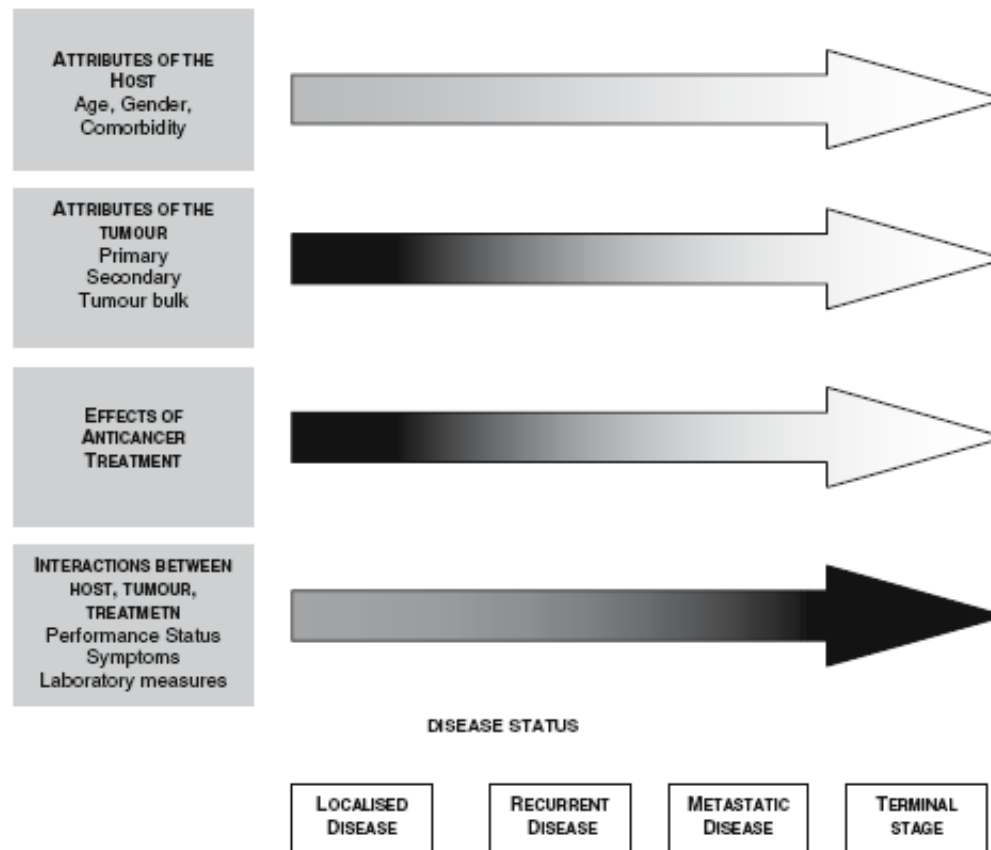


2c. Conceptual framework

adapted from Mackillop: Importance of prognosis in oncology, UICC 2001



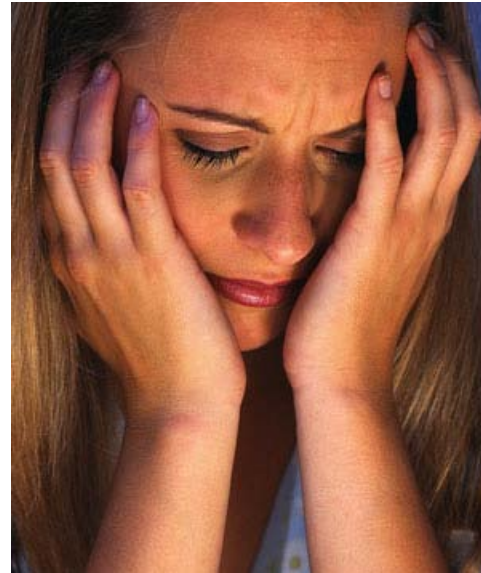
2d. Important prognostic factors depend on stage



2e. TWO TYPES OF JUDGMENT

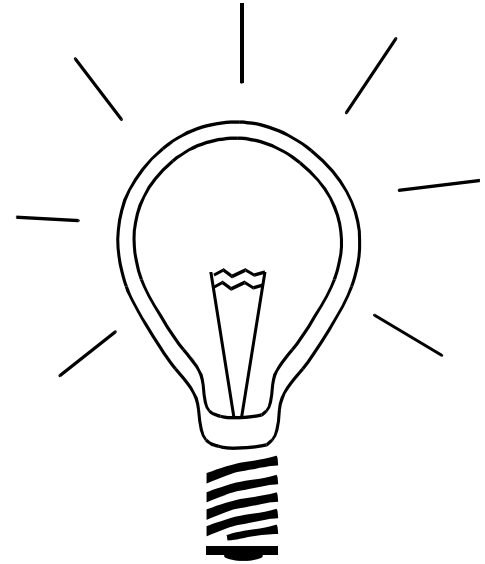
1. SUBJECTIVE/CLINICAL



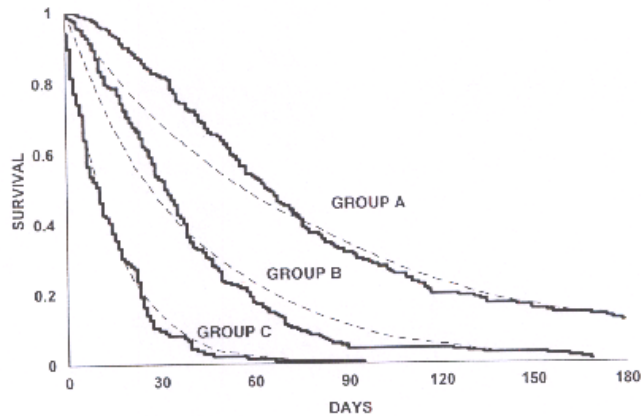


ACTUARIAL JUDGEMENT: using data/statistics to judge

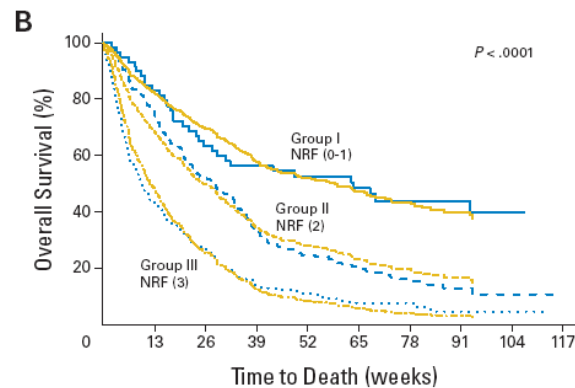
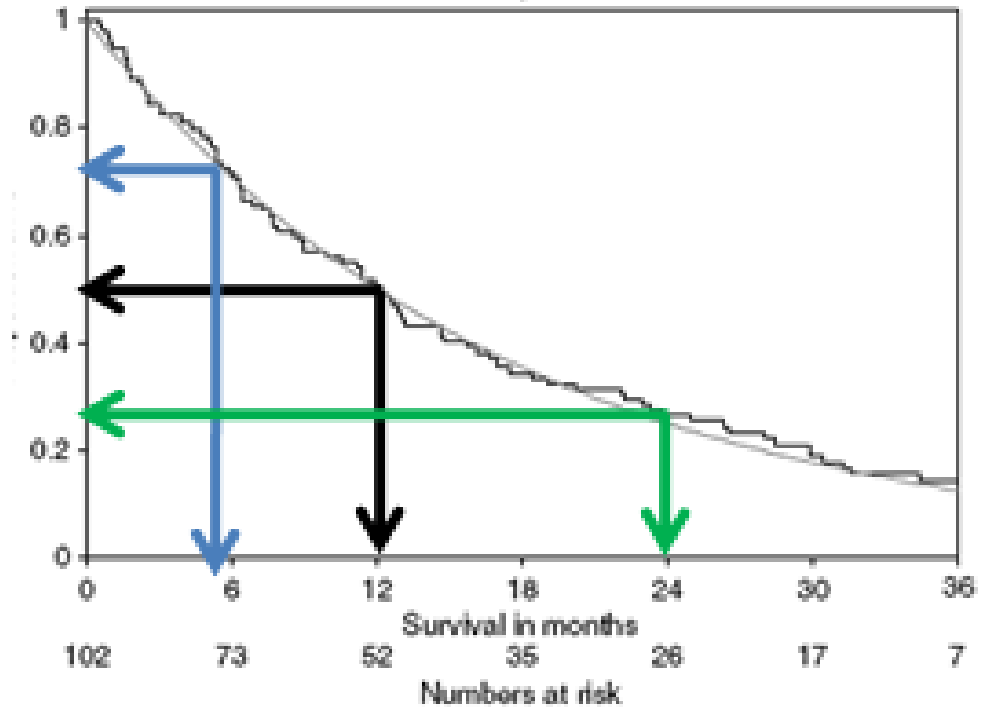
- PERFORMANCE STATUS
- SYMPTOMS
- QUALITY OF LIFE
- LABORATORY PARAMETERS



2f. Survival curves are exponential

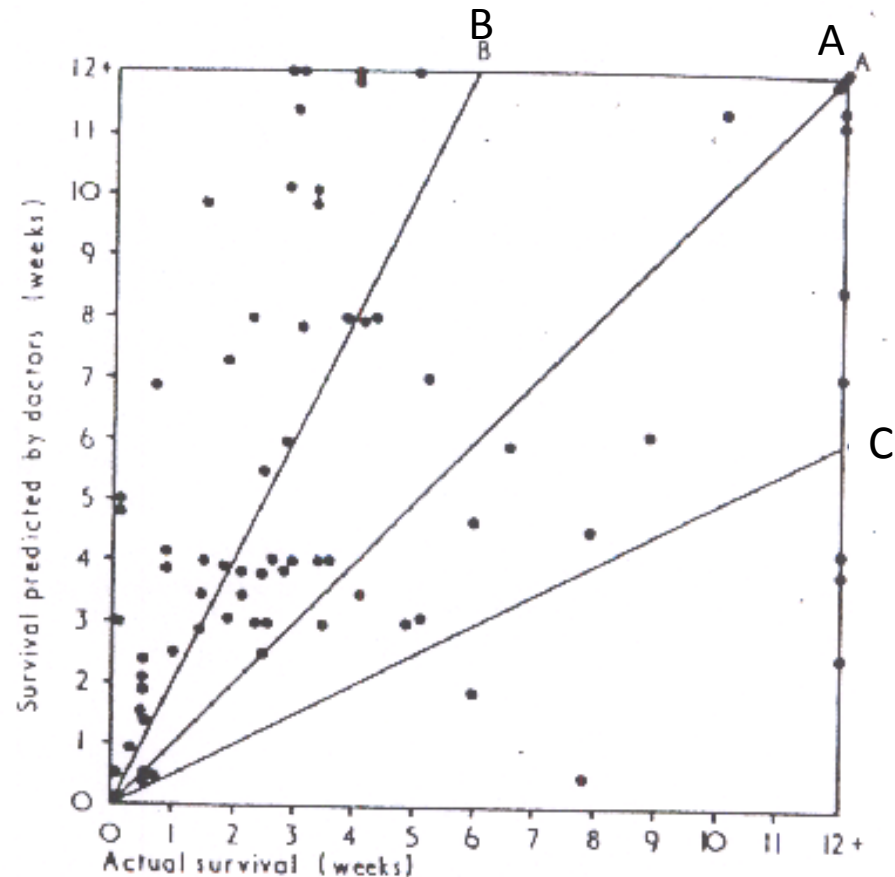


Observed and exponential survival



3. Clinical judgement: How good are physicians at prognostication?

- St.. Christopher's Hospice, London 1969-70
- prognosis estimated by referring Dr & hospice Dr
- median survival: 3.5 wk.
 - <10% accurate (A)
 - 51% out by factor of 2 (B, C)
 - 2/3 over-optimistic
- no difference between Dr's

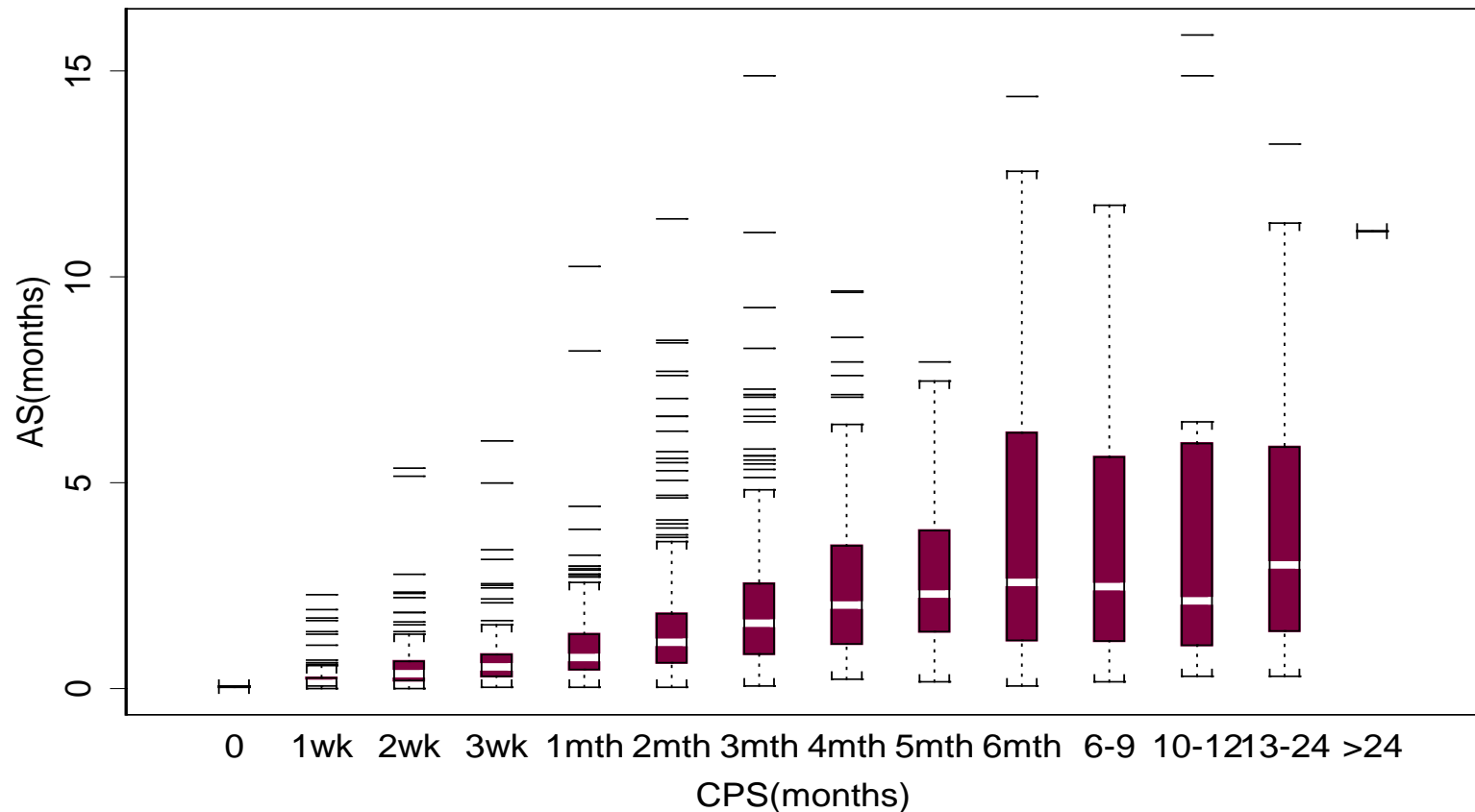


Survival predicted by doctors on day of admission by actual survival.

Parkes, BMJ 1972

Clinical predictions v. actual survival

- straight line to 6 months, then no relationship
- 1 in 4 correct (within 1 week), 1 in 4 out by > 4 weeks, and 1 in 4 do better than predicted
- narrow range in short term : horizon effect



CPS in perspective

cons

- experience
- Good memory
- Discriminative
- Well-calibrated
- dispassionate

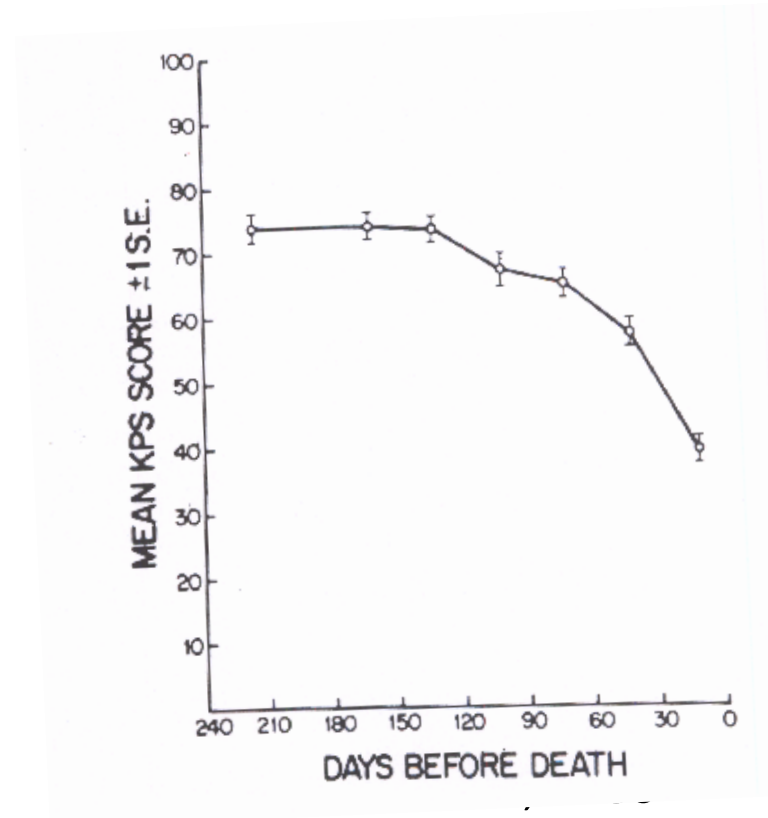
pros

- No extra data needed
- Flexibility of predictions
- Similar variance to actuarial
- Prognostic model may require it: captures “residual” data
- It’s a clinical skill!

4. ACTUARIAL JUDGEMENT

1. Performance status

- validation study of KPS
- low KPS (<50) predicts early death
 - 1/11 survived > 6 mo.
- High KPS does not predict long survival
- Rapid fall in KPS predicts death within next few mo.

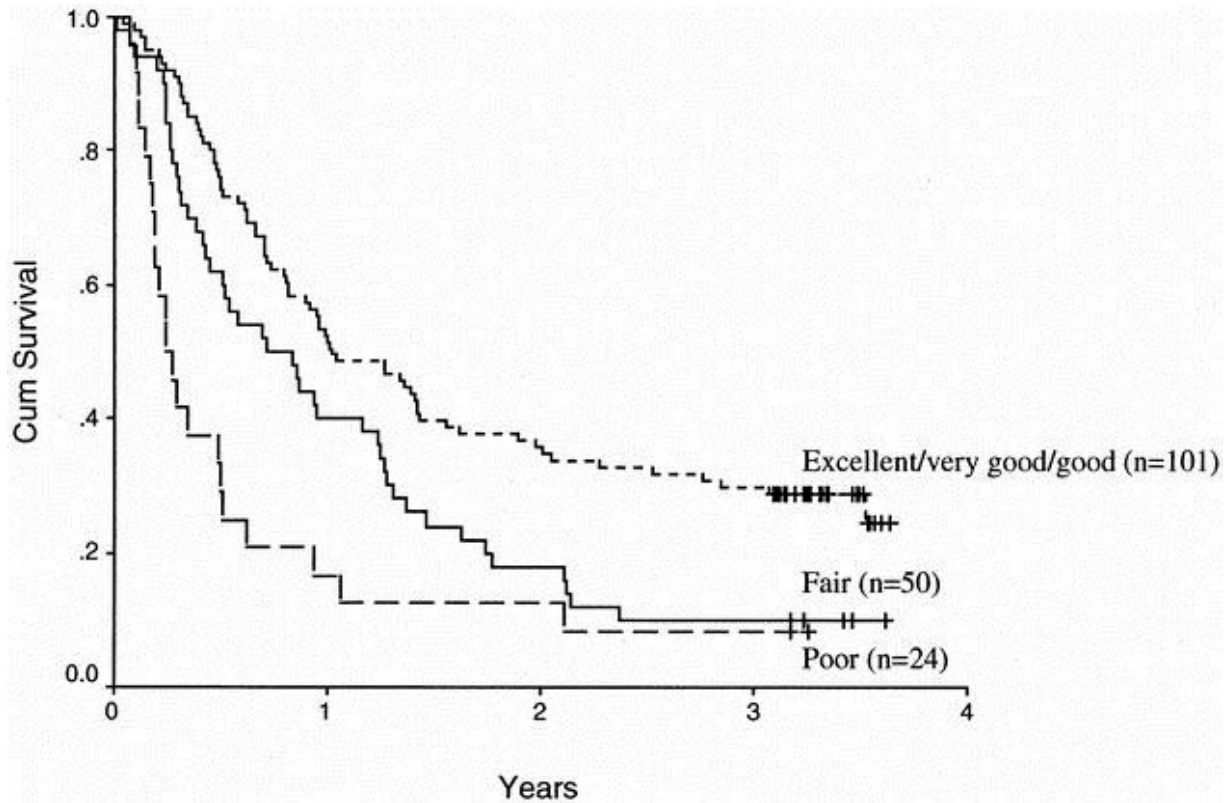


Yates, JCO 1980

2. Symptoms

- Various symptoms associated with shortened survival
 - NOT pain
 - GI: dry mouth, dysphagia, anorexia, weight loss
 - Dyspnea
 - Delirium/cognitive failure
- adding symptoms refines estimates based on KPS
 - biggest impact if $KPS > 50$

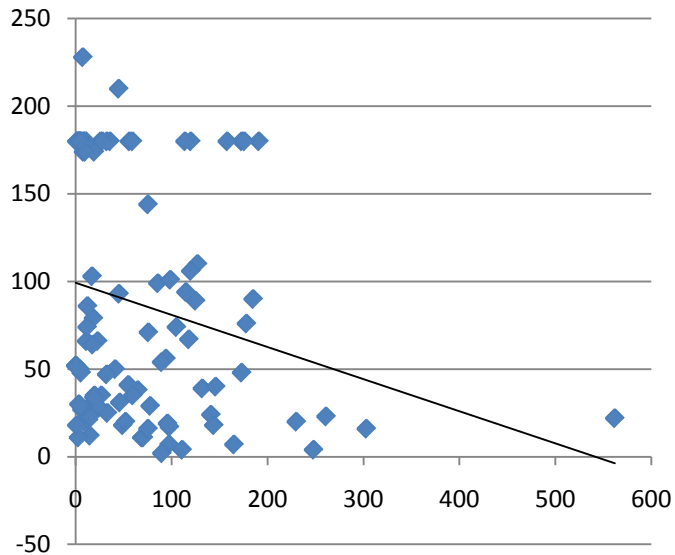
3. Quality of life and survival



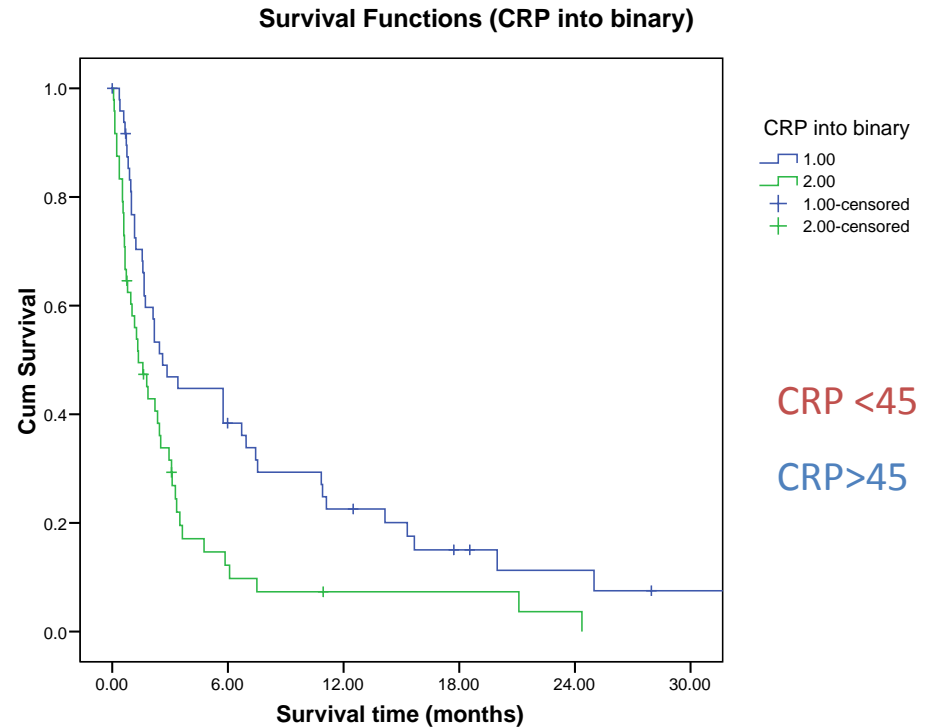
4. Laboratory parameters

- \downarrow Na; \uparrow Ca⁺⁺
- \downarrow albumin
 - acid α -glycoprotein, (pseudocholinesterase)
 - hyperbilirubinemia, LDH
- \uparrow WBC; \downarrow lymphocytes
- LDH
- **INFLAMMATORY MARKERS: CRP, CYTOKINES**

Cytokines/CRP & survival



$$r^2 = -0.241, p = 0.018$$



LRT 8.35, $p=0.004$, HR 1.89 (1.22-2.92)

5. MODELS – COMBINING FACTORS

1. Palliative Prognostic (PaP) Score

- Italian hospice-home care patients
- 36 clinical-biological variables
- Final model: probability of 30-day survival
 - symptoms: anorexia, dyspnoea
 - KPS < 30
 - labs: total WCC, total lymphocyte count
 - **clinical estimate - remained significant**

Pirovano et al JPSM 1999;17:231-239

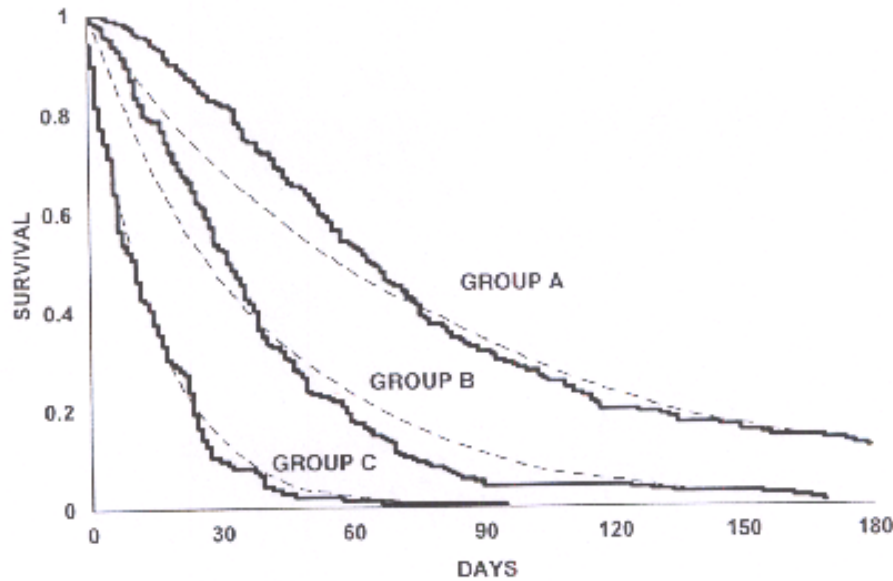
Table 5 – How to compute PaP score:⁴²

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

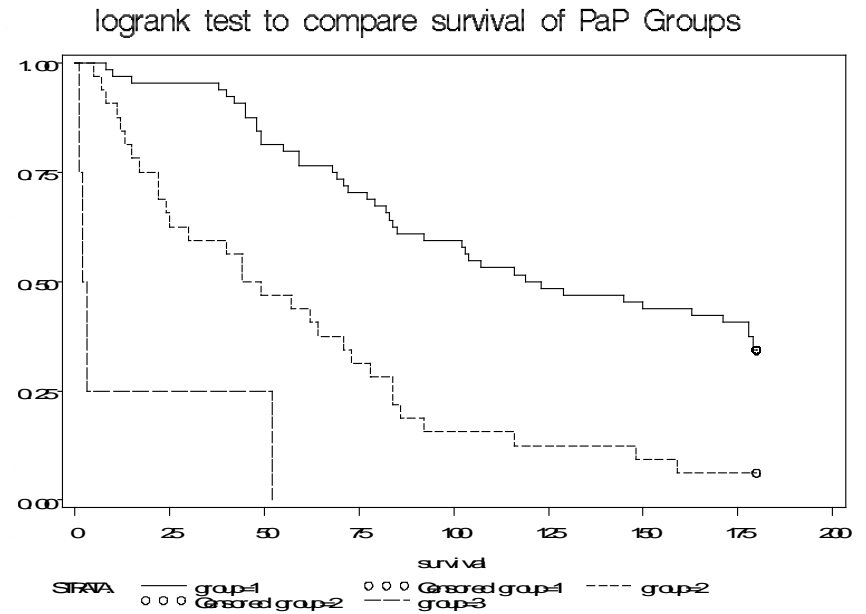
Validation studies of PaP Scores:

hospice

hospitalized oncology



Maltoni et al JPSM 1999



Glare JCO 2004

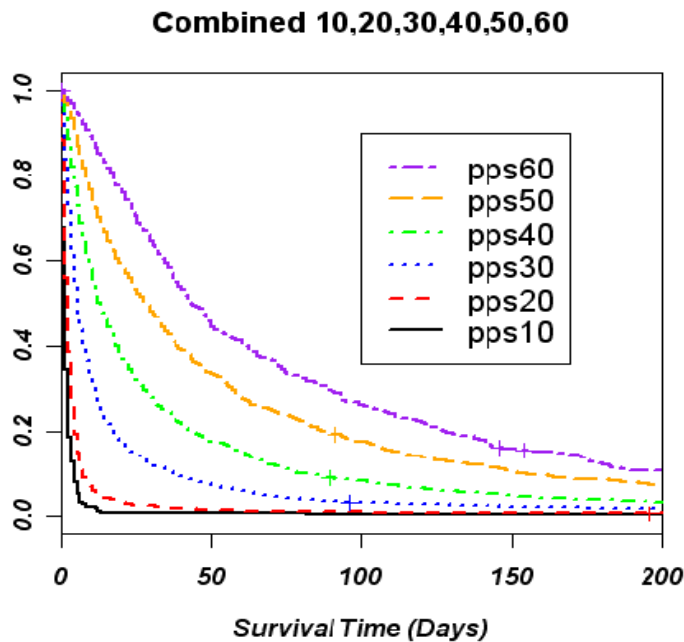
Other prognostic tools for terminal cancer (< 3 months)

| Name | Factors | prediction |
|--|---|--------------------------------|
| NHO study (US, 1985) | PS, anorexia/wt. loss, dysphagia, dry mouth, dyspnea | 50%, 10% survival (days) |
| SUPPORT model (US, 1995) | Multiple factors (like APACHE) | 6 months |
| Poor prognosis indicator (Canada, 1994) | weight loss, cognitive failure, dysphagia | <4 weeks, > 4 weeks |
| Palliative prognostic indicator (Japan, 1999) | PS, oral intake, edema, dyspnea at rest, delirium | <3,3-6, > 6 wks |
| Cancer prognostic score (Taiwan, 2004) | Liver/lung metastases, PS, weight loss, edema, delirium, fatigue, ascites | Hazard ratio |
| Intrahospital Cancer Mortality Risk Model (Turkey, 2006) | PS, short duration of illness, emergency admission, Hgb and LDH | Survive hospitalization or not |

What about ambulatory patients?

Palliative Performance Scale

Performance status first visit

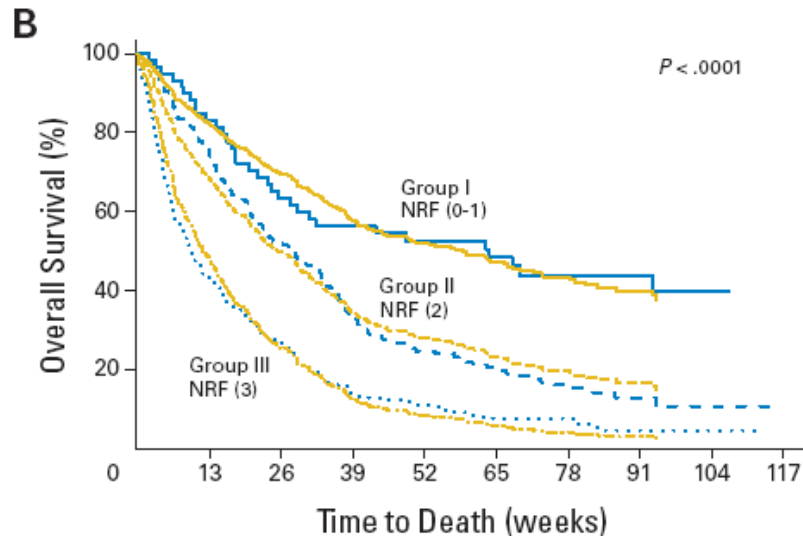


| KPS | n | died | alive | Med. |
|-----|----|----------|-------|------|
| 90 | 13 | 3 (22%) | 10 | 123 |
| 80 | 18 | 6 (33%) | 12 | 105 |
| 70 | 30 | 10 (33%) | 20 | 109 |
| 60 | 10 | 16 (62%) | 6 | 100 |
| <60 | 22 | 13 (59%) | 9 | 87 |

Simple prognostic index for ambulatory Canadian RT patients

Edward Chow

JCO 2008; 28:5863-9



One point each for:

- Non-breast cancer
- Non-ossous metastases
- KPS < 70

Median survivals

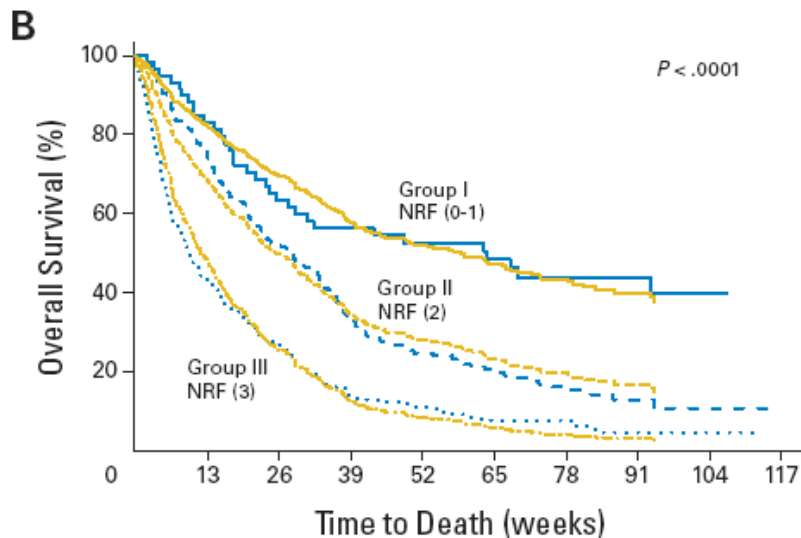
- 0-1: >12 months
- 2: 6 months
- 3: 3 months

Simple prognostic index for ambulatory Canadian RT patients

Edward Chow

JCO 2008; 28:5863-9

MSKCC PPC Clinic



| KPS | n | died | alive | Med. |
|-----|----|----------|-------|------|
| 0 | 0 | - | - | - |
| 1 | 13 | 3 (33%) | 10 | 135 |
| 2 | 49 | 17 (33%) | 32 | 106 |
| 3 | 18 | 12 (66%) | 6 | 64 |

One point each for:

- Non-breast cancer
- Non-ossous metastases
- KPS < 70

Median survivals

- 0-1: >12 months
- 2: 6 months
- 3: 3 months

Glasgow Prognostic Score (GPS)

- Hypoalbuminemia (<3.5 g/dL) = 1
- Elevated CRP (>1 mg/dL) = 1
- Scores: 0, 1, 2

Median survival (months) by GPS category

| Score/ cancer | 0 | 1 | 2 |
|--------------------------------|----|----|---|
| Gastric ¹ | 6 | 3 | 2 |
| CRC ¹ | 12 | 6 | 2 |
| NSCLC on chemo ² | 17 | 12 | 7 |
| Palliative care ³ | >6 | 2 | 1 |

1. Elahi, Nutr Cancer 2004
2. Forrest BJC 2005
3. Chiang & Glare (unpubl)

Seattle Heart Failure Model



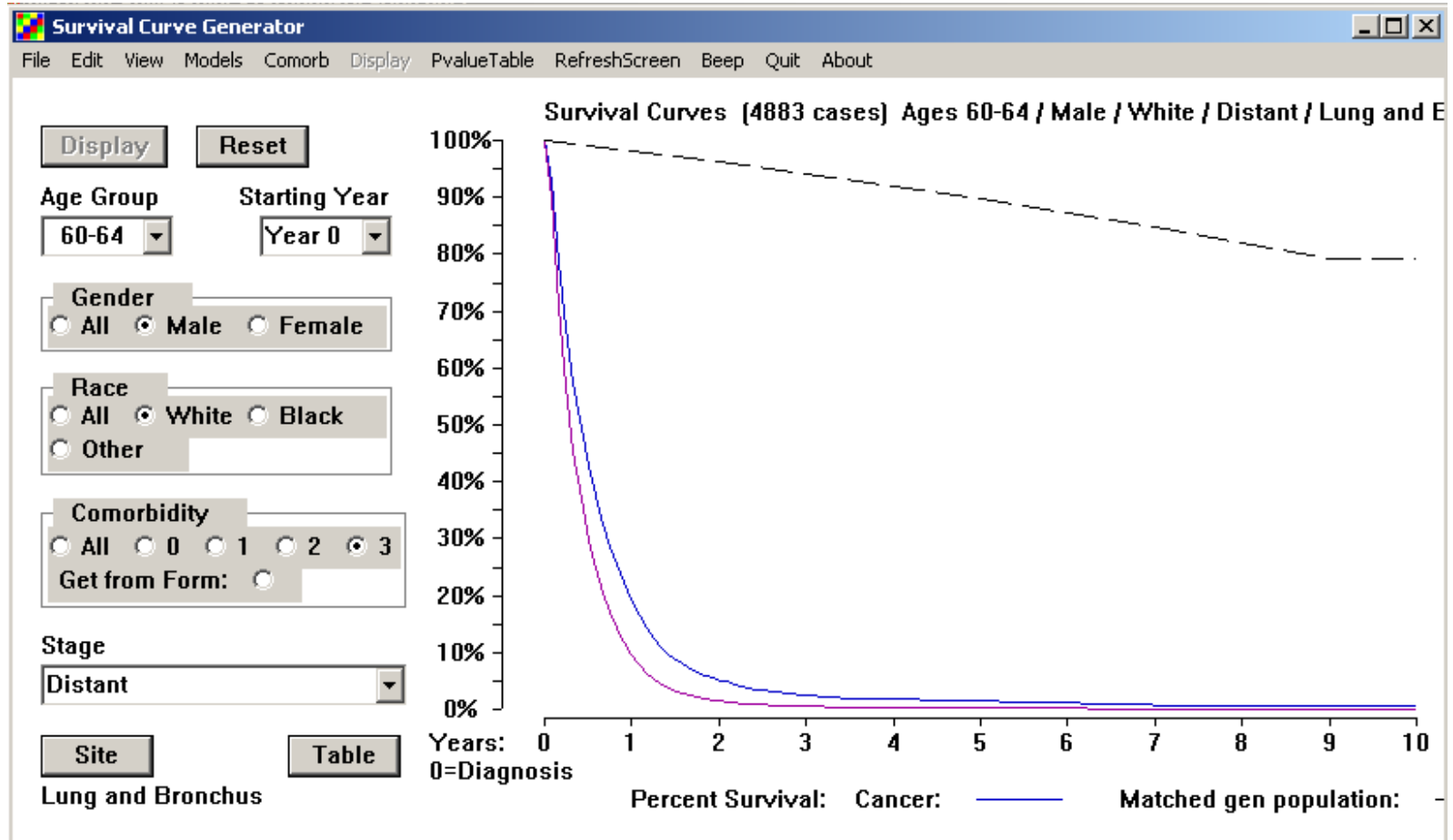
6. Communicating prognosis

- Patients want information: response to treatment, side effects, survival
- Information needs depend on age, education, culture, and will be inconsistent
- Will Get information from multiple sources
- What are they asking
 - How long

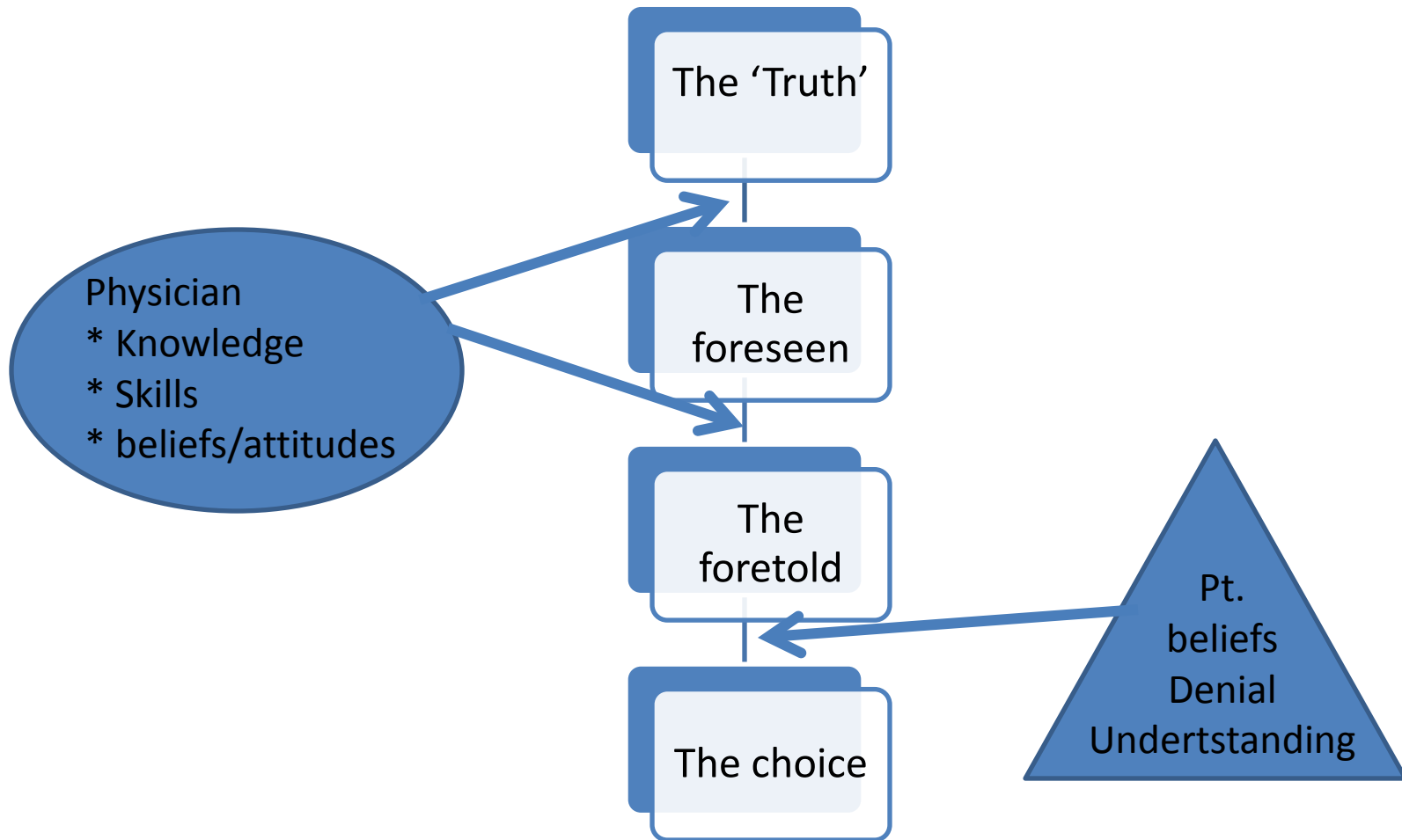
Communicating prognosis

- Generally, patients want
 - Information about prognosis and options
 - Realism with compassion
 - Hope
 - Lessening of uncertainty
- But individuals may be inconsistent and ambivalent
- Information needs affected by
 - Age
 - culture
 - Education
 - Mood
 - Proximity to death
- Patients get divergent information from multiple sources
 - Internet, relatives, other HCPs, media, etc.

Prognostigram (WUStL)



Model for prognostic communication



Patients' estimate of survival affects outcomes

| Physician Estimate of Chances for 6-mo Survival, % | Patient Estimate of Chances for 6-mo Survival, % | Proportion of Patients Favoring Life-Extending Therapy | Odds Ratio (95% CI)† |
|--|--|--|----------------------|
| ≥90 | ≥90 | 20/36 | 0.83 (0.12-5.6) |
| | <90 | 3/5 | |
| 61-89 | ≥90 | 34/66 | 2.6 (0.81-8.0) |
| | <90 | 5/17 | |
| 40-60 | ≥90 | 58/130 | 1.7 (0.90-3.2) |
| | <90 | 21/65 | |
| 11-39 | ≥90 | 31/54 | 3.5 (1.6-7.8) |
| | <90 | 15/54 | |
| ≤10 | ≥90 | 23/38 | 8.5 (3.0-24.0) |
| | <90 | 7/46 | |
| Total | ≥90 | 198/390 | 2.6 (1.8-3.7) |
| | <90 | 61/216 | |

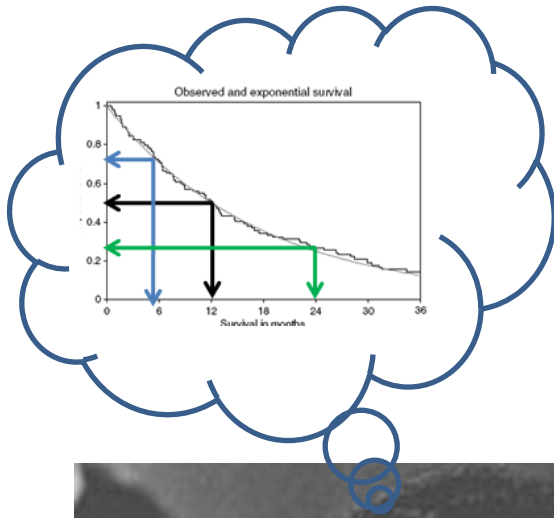
- if >90% chance at 6 months , 2.6 times more likely to request life prolonging therapies than palliative care
- No difference in survival
- More likely to have a bad outcome (e.g. die in ICU)

7. Answering Mary Smith I



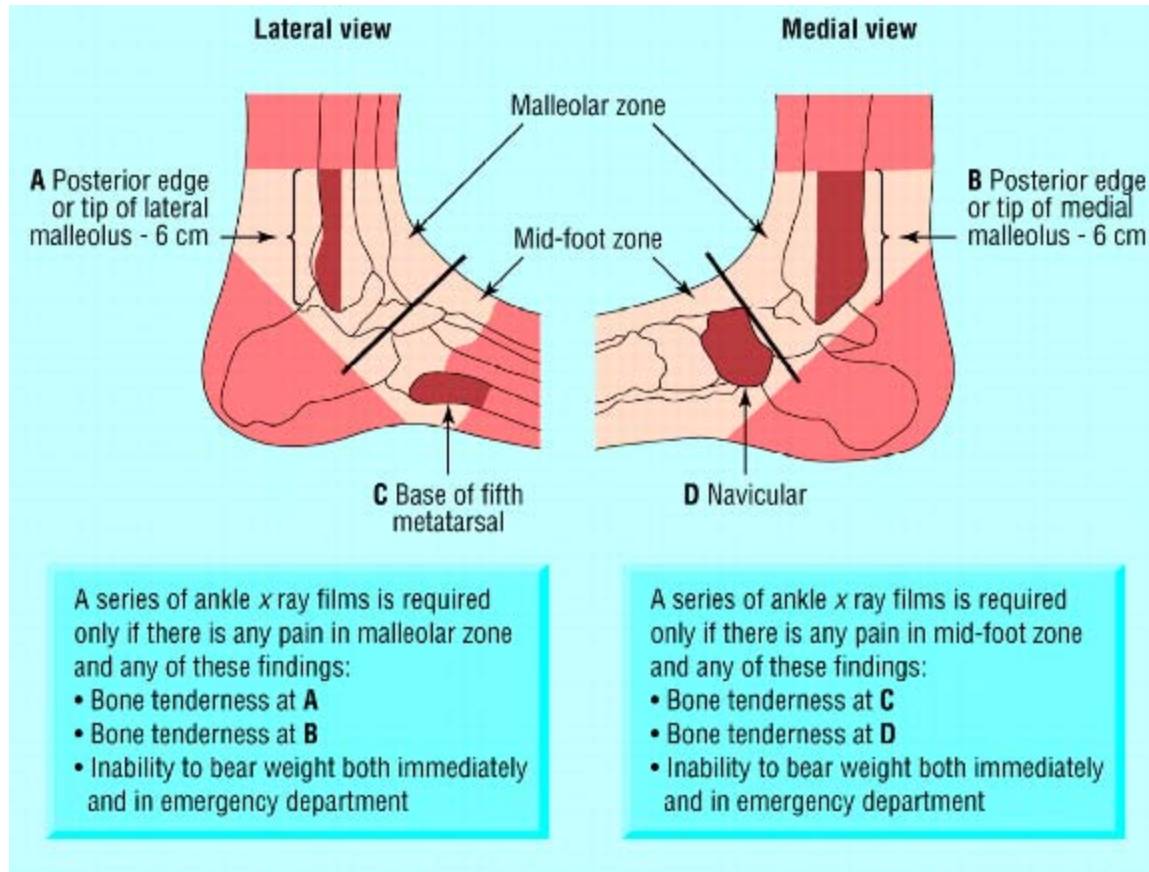
You have 1
month to live

Answering Mary Smith II



If we had 100 people like you, we would expect the 10 who did best to still be around in 3-4 months and the 10 who did worst to be in trouble as soon as next week

8. Future: Prognostic tools as clinical decision aids ?



summary

- Prognosis became undervalued as a clinical skill in the 20th century and is not well developed
- There have been advances in foreseeing but it is still inaccurate
- Poor foretelling leads to bad decision making
- Not much point improving foreseeing and foretelling if not going to use it to change decisions