Prognostic factors in patients with advanced cancer: the use of the Patient-Generated Subjective Global Assessment in survival prediction

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Conceptual model of cancer death trajectory

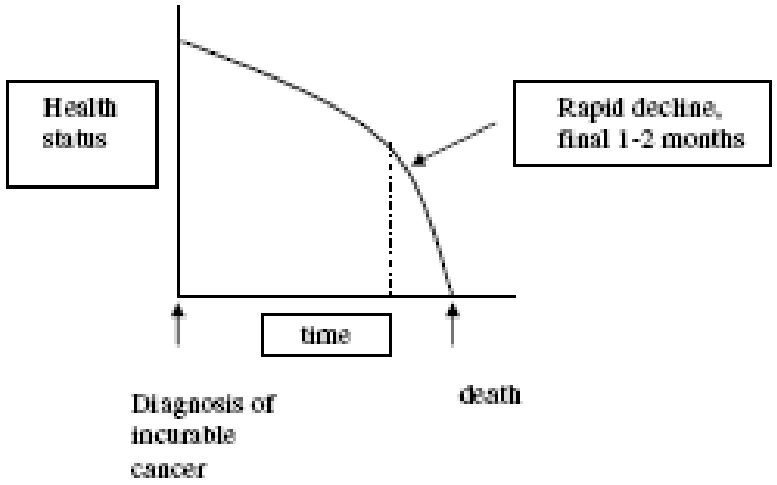

Fig. 1 – Conceptual model of cancer death trajectory.[122,123]

Barb Tarbox 1961 - 2003

What constitutes *timely*?

- Patient view

  - Vital opportunity to consider planning, priorities and preparation for death
  - Informed choices of treatment options and place of care
  - Establish eligibility for care programs, Palliative benefit plan, EI for family caregiver

- Health Services view

  - Recommendation of treatment options and place of care
  - Allocation of scarce resources

The bases of prediction

- Clinical prediction by health care professionals
  - Opinion of specialist physician, hospital or family physician nurse, care aid.
- Statistical estimate based on data
  - Based on empirical data: disease and demographic, performance status, symptoms, quality of life, biological parameters… at least 150 different variables have been used in survival prediction

Notion of *timeliness* is based on *Prognostication* defined as clinical prediction of:

- **Disease progression or recurrence**
- **Disability or discomfort**
- **Drug toxicity**
- **Likelihood of completing participation in research**
- **Use or cost of health care services**
- **Death**

Clinical prediction of survival- how good is it?

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Prediction of Patient Survival by Healthcare Professionals in a Specialist Palliative Care Inpatient Unit: A Prospective Study

Feargal Twomey, MB, MRCPI, Norma O'Leary, MB, MRCPI, and Tony O'Brien, MB, FRCPI

- Less than 24 hours
- Greater than 24 hours but less than 72 hou
- Greater than 72 hours but less than 10 day
- Greater than 10 days but less than one mo
- Greater than one month but less than three m
- Greater than three months

Table 2. Accuracy of Survival Prediction by Group

Group	n	Weighted Kappa[a]	95% Confidence Interval
For all 221 patients			
Nurse Managers	191	0.48	(0.39,0.56)
Nurses	196	0.48	(0.39,0.56)
Care assistants	180	0.36	(0.27,0.46)
Consultant	148	0.41	(0.31,0.51)
NCHDs	200	0.47	(0.39,0.56)

Clinical estimation of survival by radiation oncologists

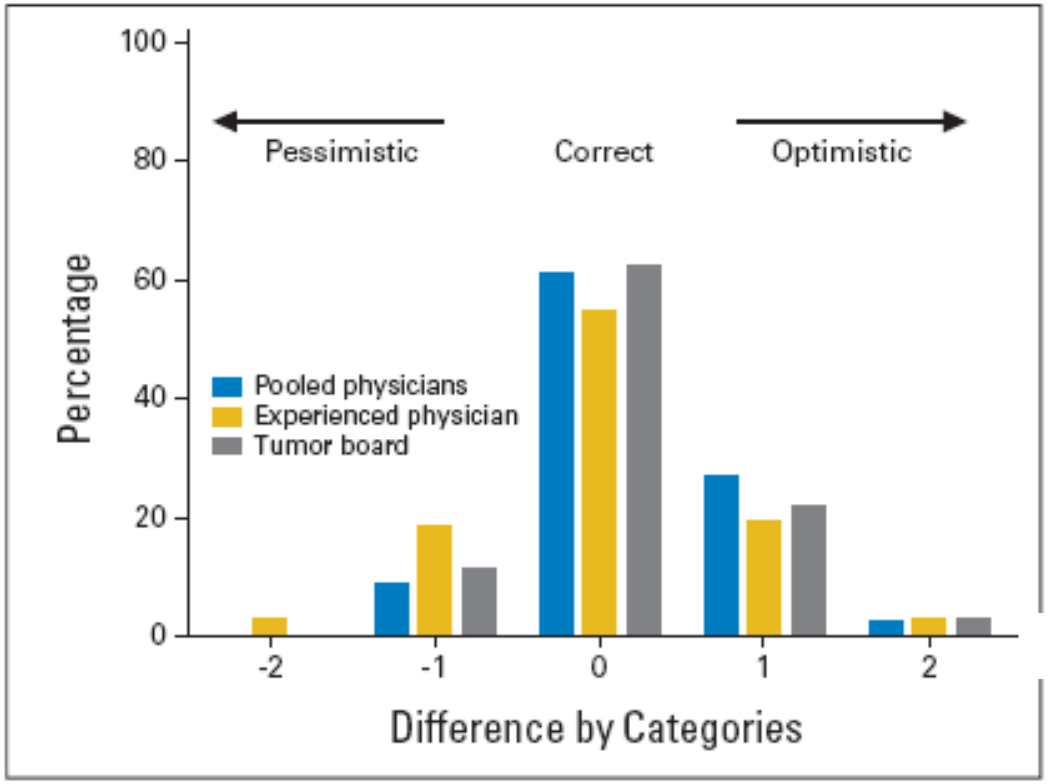

Fig 1. Discrepancy between actual and predicted survival by survival categories. Minus 2 means an underestimation of survival by two categories (ie, the prognosis was too pessimistic).

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ORIGINAL REPORT

Clinical prediction of survival..

- Clinical prediction of survival by all categories of health care providers is inaccurate. (*ie* explains much less than half of the variation in actual survival)
- Most health care providers feel poorly trained to both formulate and communicate a prognosis of death
- Stress and worry connected with inaccurate predictions.
- Coping strategies include avoidance, optimism, vagueness

Statistical estimates of survival:

- Based on empirical data: disease and demographic, performance status, symptoms, quality of life, biological parameters… at least 150 different individual variables have been used in survival prediction

(if you happen to maintain good quality data sets on your patients)

Data considered

- Oncology
- TNM Stage
- Treatment intervention
- Performance status
- Number and location of metastases
- Blood and laboratory features
- Nutritional status
- Prognostic scores

- Palliative Medicine
- Physician –estimated survival
- Performance status
- Pain and Symptoms
- Blood and laboratory work
- Nutritional status
- Psychosocial
- Palliative Prognostic scores

Predicting survival in patients with advanced disease (<90 d)

Paul Glare[a,b,*], *Christian Sinclair*[c,d,j], *Michael Downing*[e,f], *Patrick Stone*[g], *Marco Maltoni*[h], *Antonio Vigano*[i]

Table 3 – The extent to which various clinical variables appear to be predicative of survival in patients with far advanced cancer[121]

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

a Positive on either univariate or multivariate analysis.

Table 7. Palliative Prognostic Score*

Prognostic Factor	Partial Score
Dyspnea	
Absent	0
Present	1
Anorexia	
Absent	0
Present	1.5
Karnofsky performance status	
≥ 50	0
30-40	0
10-20	2.5
Clinical prediction of survival	
> 12 weeks	0
11-12 weeks	2.0
9-10 weeks	2.5
7-8 weeks	2.5
5-6 weeks	4.5
3-4 weeks	6.0
1-2 weeks	8.5
Total WBC count (cell/mm^3)	
Normal: 4,800-8,500 cells/μL	0
High: 8,501-11,000 cells/μL	0.5
Very high: > 11,000 cells/μL	1.5
Lymphocyte percentage	
Normal: 20.0%-40.0%	0
Low: 12.0%-19.9%	1.0
Very low: 0%-11.9%	2.5

NOTE. The risk groups and total scores were as follows: group A: 30-day survival probability of > 70%, score = 0 to 5.5; group B: 30-day survival probability of 30% to 70%, score = 5.6 to 11.0; and group C: 30-day survival probability of < 30%, score = 11.1 to 17.5.
*Palliative Prognostic Score = dyspnea score + anorexia score + Karnofsky performance status score + clinical prediction of survival score + total WBC count score + lymphocyte percentage score.

Palliative Prognostic Score

A prognostic scoring system based on Clinical Prediction, Karnofsky performance, symptoms and blood work.

Palliative Performance Scale (PPSv2) *version 2 (developed by Victoria Hospice Society)*

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 *with* 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	Drowsy or Coma +/- Confusion
0%	Death	-	-	-	-

*Home is defined as the patient's usual residence (may include long term care facility)

A salad of prognostic tools……

- Palliative prognostic score (PaP)
- Palliative Performance Index (PPI)
- Palliative performance scale (PPS)
- Cancer prognostic score
- Intrahospital cancer mortality risk model (ICMRM)
- Glasgow Prognostic Score
- Prognostat

Palliative instruments

- Based on different input data
- Data may be specific to one care setting
- Some small convenience samples; few large, population –based data sets of high quality
- Pragmatic clinical information-based
- Based on lab tests, new research measures (ie interleukin-6)
- No common minimum data set

Nutrition and Prognostication

- Many prognostication instruments contain a nutrition – related element on dietary intake
- The nutrition elements are often weak – it has not been established that they are indeed the most prognostic variables and the quantification of “anorexia” is vague

Nutrition elements

- PGSGA Nutrition Instrument
- RD – Oncology recommended tool
  - Weight history, body mass index
  - Food intake score
  - “Nutrition Impact” symptoms YES/NO
  - Functional status score = Eastern Clinical Oncology Group ECOG score

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

History (Boxes 1-4 are designed to be completed by the patient.)

1. Weight *(See Worksheet 1)*

In summary of my current and recent weight:

I currently weigh about _____ pounds
I am about _____ feet _____ tall

One month ago I weighed about _____ pounds
Six months ago I weighed about _____ pounds

During the past two weeks my weight has:

☐ decreased (1) ☐ not changed (0) ☐ increased (0) Box 1 ☐

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

History (Boxes 1-4 are designed to be completed by the patient.)

2. Food Intake: As compared to my normal intake, I would rate my food intake during the past month as:

- ☐ unchanged (0)
- ☐ more than usual (0)
- ☐ less than usual (1)

I am now taking:

- ☐ *normal food* but less than normal amount (1)
- ☐ little solid food (2)
- ☐ only liquids (3)
- ☐ only nutritonal supplements (3)
- ☐ very little of anything (4)
- ☐ only tube feedings or only nutrition by vein (0)

Box 2 ☐

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

History (Boxes 1-4 are designed to be completed by the patient.)

3. Symptoms: I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply):

- ☐ no problems eating (0)
- ☐ no appetite, just did not feel like eating (3)
- ☐ nausea (1)
- ☐ constipation (1)
- ☐ mouth sores (2)
- ☐ things taste funny or have no taste (1)
- ☐ problems swallowing (2)
- ☐ pain; where? (3)_____
- ☐ other** (1) _____
- ☐ vomiting (3)
- ☐ diarrhea (3)
- ☐ dry mouth (1)
- ☐ smells bother me (1)
- ☐ feel full quickly (1)
- ☐ fatigue (1)

** Examples: depression, money, or dental problems

Box 3 ☐

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

History (Boxes 1-4 are designed to be completed by the patient.)

4. Activities and Function: Over the past month, I would generally rate my activity as:

- ☐ normal with no limitations (0)
- ☐ not my normal self, but able to be up and about with fairly normal activities (1)
- ☐ not feeling up to most things, but in bed or chair less than half the day (2)
- ☐ able to do little activity and spend most of the day in bed or chair (3)
- ☐ pretty much bedridden, rarely out of bed (3)

Box 4 ☐

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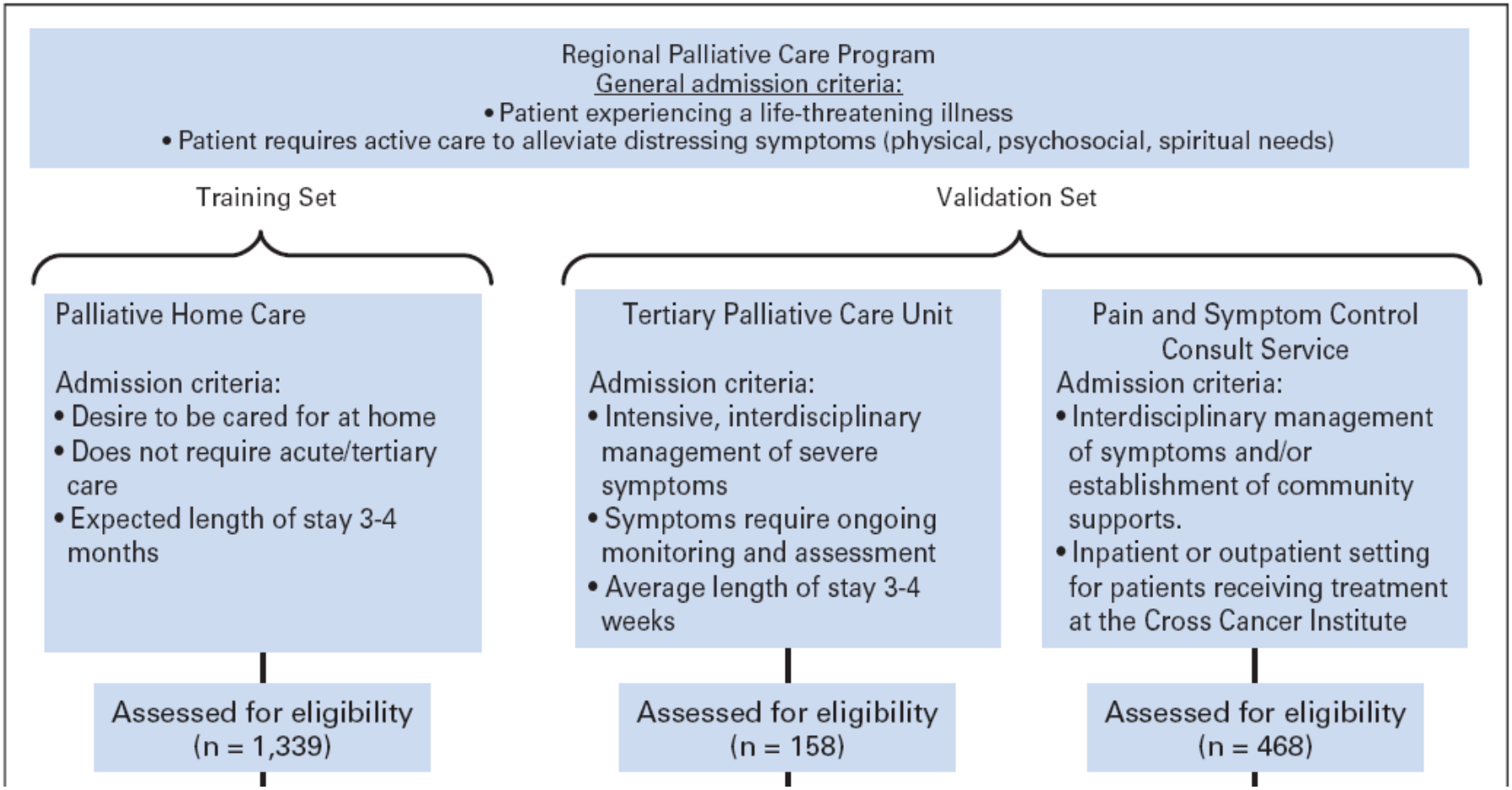
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Prognostic Factors in Patients With Advanced Cancer: Use of the Patient-Generated Subjective Global Assessment in Survival Prediction

Lisa Martin, Sharon Watanabe, Robin Fainsinger, Francis Lau, Sunita Ghosh, Hue Quan, Marlis Atkins, Konrad Fassbender, G. Michael Downing, and Vickie Baracos


Regional Palliative Care Program
General admission criteria:
• Patient experiencing a life-threatening illness
• Patient requires active care to alleviate distressing symptoms (physical, psychosocial, spiritual needs)
Training Set
Validation Set
Palliative Home Care
Admission criteria:
• Desire to be cared for at home
• Does not require acute/tertiary care
• Expected length of stay 3-4 months
Tertiary Palliative Care Unit
Admission criteria:
• Intensive, interdisciplinary management of severe symptoms
• Symptoms require ongoing monitoring and assessment
• Average length of stay 3-4 weeks
Pain and Symptom Control Consult Service
Admission criteria:
• Interdisciplinary management of symptoms and/or establishment of community supports.
• Inpatient or outpatient setting for patients receiving treatment at the Cross Cancer Institute
Assessed for eligibility (n = 1,339)
Assessed for eligibility (n = 158)
Assessed for eligibility (n = 468)

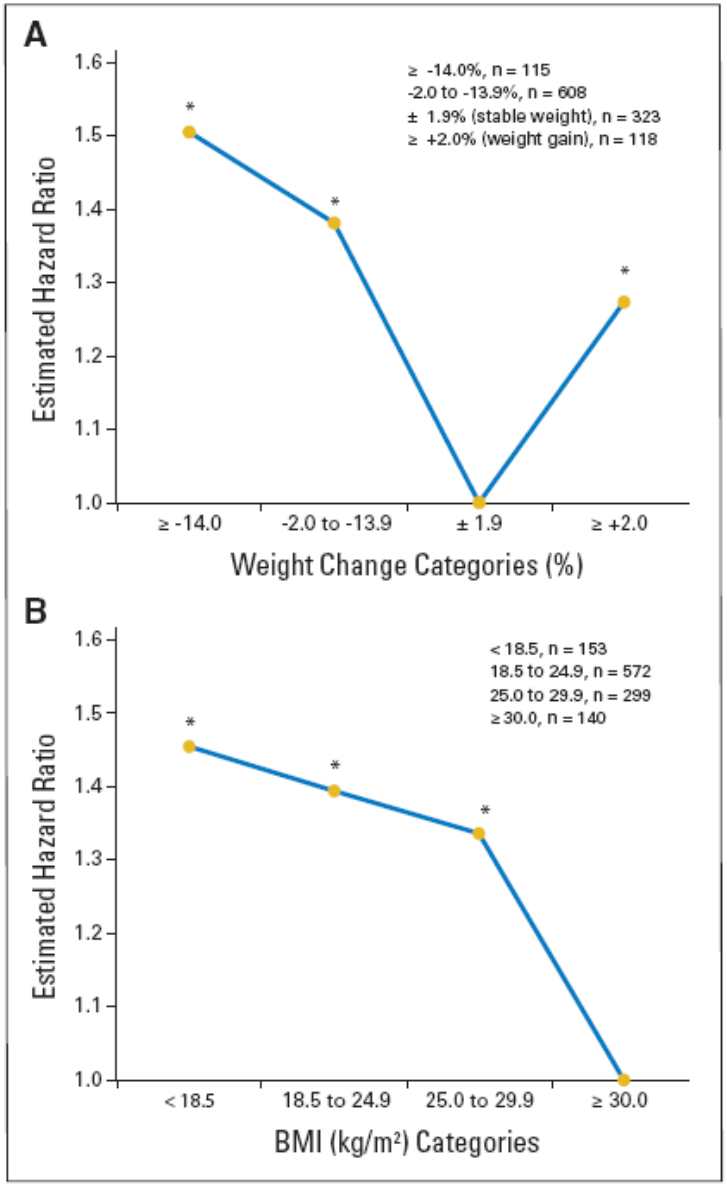


Fig 2. Univariate relationship between survival and (A) percent weight change categories (reference group: stable weight ± 1.9%; hazard ratio 1.0 refers to the lowest risk of shortened survival) and (B) body mass index (BMI; kg/m^2) WHO categories (reference group: largest BMI, ≥ 30.0; hazard ratio, 1.0). (*) Indicates significant difference from reference group ($P < .05$).

Univariate analysis of Body mass index and weight loss, some surprises:

- Mean BMI 24.0±5.3 closer to overweight than underweight
- BMI > 30 (obese) predicts longer survival
- Weight loss relationship U-shaped, short term weight gain a poor prognostic factor

.

Predicted survival in multivariate analysis

- Cancer site
- ECOG performance (patient – self rated)
- Weight loss or weight gain
- Food intake
  - Little solid food
  - Only liquids
  - Very little of anything
- Dysphagia

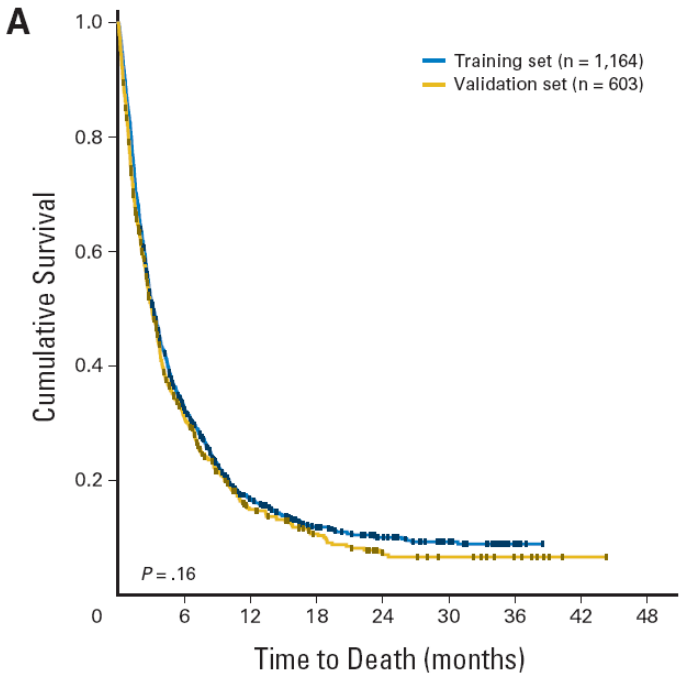
Testing the model: concordance statistics

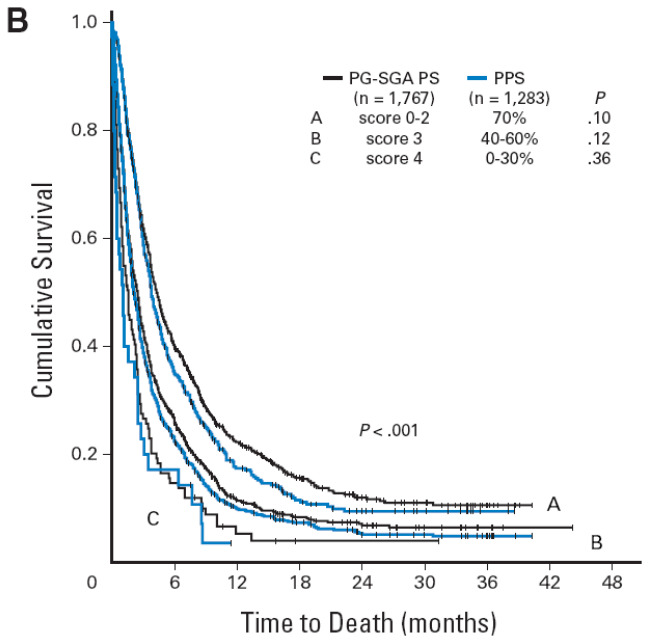
- C-stats were used to test the predictive accuracy of models based on the trainining and the validation data sets
- C-stat is the probability that a participant from an event group (ie a group with a poor prognostic factor) has a higher risk of an event (ie death) than a participant from a non-event group.
- C-stat of 0.50 means that the model predicts the outcome as well as chance; 1.00 is a perfect prediction.
- Structured sort of like a “bet” where each patients’ actual survival is compared with their predicted survival.

Table 3. Discrimination of Overall Survival for a Predictive Model in a Training and Validation Set and for Two Measures of Functional Status

Variable	Training Set (n = 1,164)		Validation Set (n = 603)		PG-SGA PS‡ (n = 1,767)	PPS‡ (n = 1,283)
	Base Model*	Full Model†	Base Model*	Full Model†		
C-statistic	0.90	0.88	0.88	0.87	0.93	0.93
95% CI	0.86 to 0.93	0.83 to 0.91	0.82 to 0.93	0.80 to 0.92	0.90 to 0.96	0.90 to 0.96

NOTE. There are no statistical differences between concordance statistics (c-statistics; $P > .05$).
Abbreviations: PG-SGA PS, patient-generated Subjective Global Assessment performance status; PPS, Palliative Performance Scale.
*Base model includes cancer diagnosis and functional status.
†Full model includes cancer diagnosis, functional status, percent weight change, dietary intake, and dysphagia.
‡The calculations of c-statistics were performed on PG-SGA PS and PPS only (ie, no other variables were included).





Variable	Lung and GI Cancers				
	No. of Patients	No. of Events	Median Survival (months)	95% CI	*P**
Patient-reported PG-SGA PS (n = 1,767)					
0-2	442	372	3.7	3.3 to 4.1	< .001
3	419	377	2.0	1.6 to 2.3	
4	51	51	1.0	0.5 to 1.5	
Physician-reported PPS (n = 1,283)					
≥ 70%	222	202	3.4	2.9 to 3.8	< .001
40%-60%	419	386	1.8	1.6 to 2.1	
0%-30%	13	13	0.3	0.2 to 0.5	

Conclusions

- Prognostic nutrition information
  - Nutrition information prognostic, in unanticipated ways.
  - Potential dual use of nutrition screening tools: nutrition risk assessment and prognostication
- Populations, data sets
  - Population –based data sampling, appropriate stats
- Patient – generated information of value
  - Think about prognostic tools in terms of cost, time spent, invasiveness – necessary?
- Pretty good, but not perfect predictive models
  - Taking bets? How to refine the predictions that we have?

Future Hope

- Assembly of important data sets
- Reduce the number of assessements
- Prediction with high accuracy
- Timely access to end of life care