How useful are prognostic scores in clinical practice?

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Recommendation # 5

- **A number of prognostic scores or indices have been developed which are easy to use and allow a rapid estimate of life expectancy by placing patients into broad groups which differ significantly in survival (A).**

Estimate of survival of patients admitted to a Palliative Care Unit: a prospective study

(Bruera, JPSM,1992)

- **61 pts (47 evaluable)**
- **13 variables**
- **Dysphagia: log reg p=0.003; RR=22.4**
- **Cognitive failure: log reg p=0.02; RR=10.5**
- **Weight loss: log reg p=0.03; RR=12**
- **Poor Prognostic Indicator: similar specificity, sensitivity, and overall accuracy , but higher level of significance than physicians' estimates (0.0001 vs 0.008 vs 0.14) in predicting survival more or less than 4 wk**

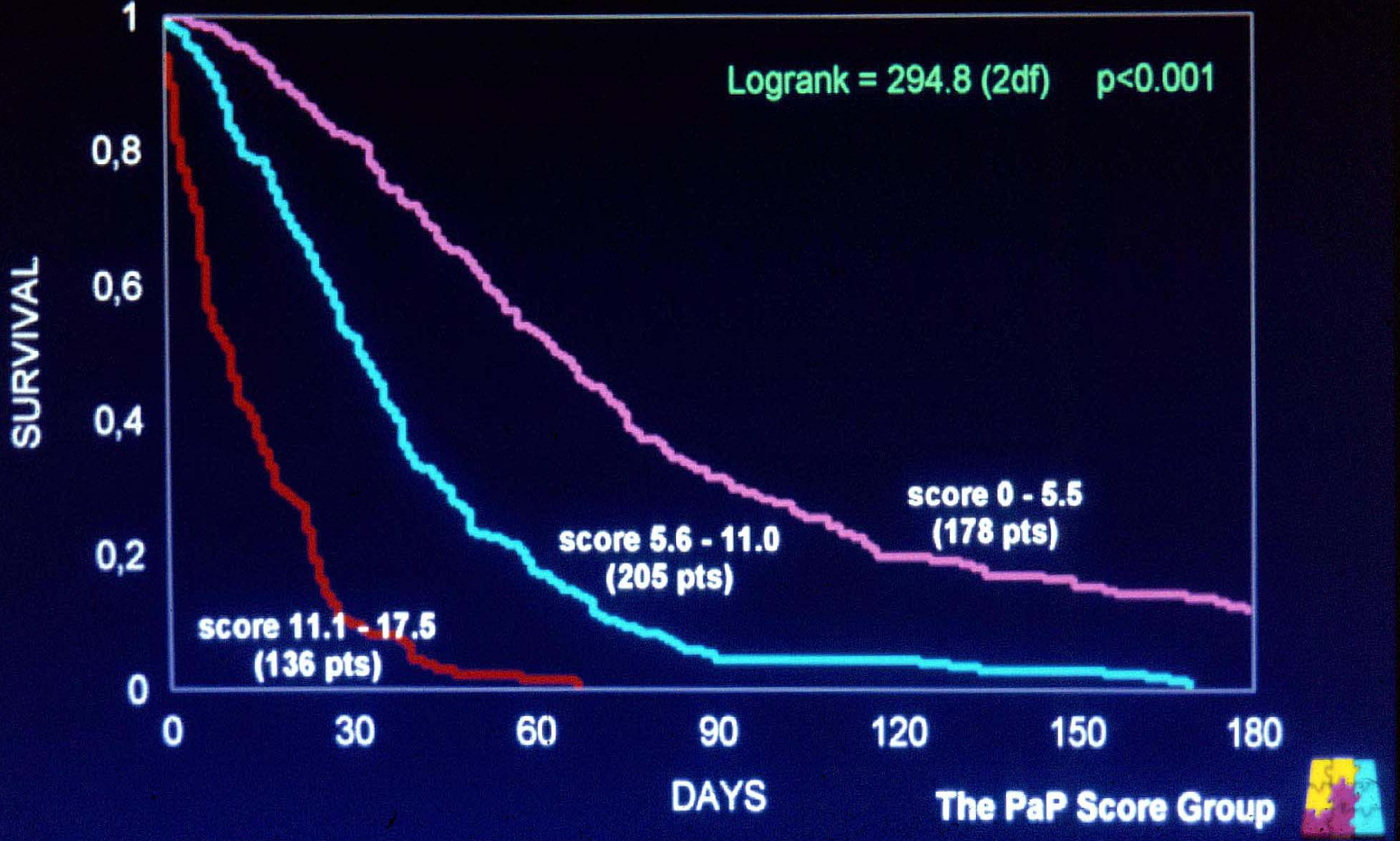
THE PALLIATIVE PROGNOSTIC SCORE (PaP Score)

Characteristic	Score	Characteristic	Score
Dyspnea		Karnofsky Performance Status	
No	0	≥50	0
Yes	1	30-40	0
Anorexia		10-20	2.5
No	0	Total leukocytes (cell mm^3)	
Yes	1	4800-8500	0
Clinical prediction of survival (wks)		8501-11000	0.5
>12	0	>11000	1.5
11-12	2.0	Lymphocyte rate (%)	
9-10	2.5	20.0-40.0	0
7-8	2.5	12.0-19.9	1.0
5-6	4.5	0-11.9	2.5
3-4	6.0		
1-2	8.5		

PaP Score groups according to their 30-day survival probability estimate

Risk group		30-days survival (%)	PaP Score
A.	Best prognosis	>70	0.0-5.5
B.	Intermediate prognosis	30-70	5.6-11.0
C.	Worst prognosis	<30	11.1-17.5

TRAINING SET: Survival experience of the three groups of patients identified by the prognostic score of 519 patients.



The Palliative Prognostic Index: a scoring system for survival prediction of terminally ill cancer patients

(Morita,SCC,1999)

	Regression coefficient +/- standard error	Partial Score Value
PPS		
10-20	1.0+/-0.26*	4.0
30-50	0.60+/- 0.17*	2.5
>=60	0.0	0
Clinical symptoms		
Oral intake		
Severely reduced	0.63+/-0.18*	2.5
Moderately reduced	0.26+/-0.14*	1.0
Normal	0.0	0
Edema	0.31+/-0.13**	1.0
Dyspnea at rest	0.88+/-0.16*	3.5
Delirium	1.0+/-0.17*	4.0

*p<0.01, **p<0.05

Prognostic factors in prognostic scores

		CACS sign or symptom	Mental status	Dyspnea	PS	Others
Bruera	1992	Dysphagia Weight loss	Cognitive failure			
Pirovano	1999	Anorexia		Y	KPS	CPS WBC+ Lym-
Morita	1999	Oral intake	Delirium	Y	PPS	Edema
Yun	2001	Anorexia	Confusion			Diarrhea

Diagnostic accuracy of the Palliative Prognostic Score in hospitalized patients with advanced cancer

(Glare, JCO, 2004)

- **100 inpatients**
- **PaP Score: three groups: 17 weeks (12-26), 7 (4-12), <1(<1-3)**
- **1-month survival: 97%, 59%, 25%**
- **Statistically significant survival differences: p<.001**

Decision making process for switching from cure to care

- Life expectancy (prognostic factors)
- Patient characteristics (age, PS, awareness, psychological and spiritual attitude)
- Patient wishes
- Current and expected quality of life
- Features of the tumor (biological pattern)
- Expected toxicity from conventional therapies
- Availability of experimental drugs
- Economic considerations

Trends in aggressiveness of cancer care near the end of life

(28,777 pts 65 ys+ dead in 1 y)

	1993	1996	p
Chemo last 2 weeks	13.8	18.5	<.001
Emergency dept visit last month	7.2	9.2	<.001
Hospitalization last month	7.8	9.1	=.008
Admission ICU last month	7.1	9.4	=.009
Last 3 days hospice	14.3	17.0	=.004
Acute care hospital death	32.9	29.5	<.001
Hospice service use	28.3	38.8	<.001

Earle, JCO,2004

Physician factors in the timing of cancer patient referral to Hospice Palliative Care

(Lamont, Cancer 2002; 94:2733)

- 326 patients, median survival 26 days

- 2 or more pts last three months = +17
- Accurate survival estimate = +20
- Internist and geriatrician = +18 than oncologists

EXTENT AND DETERMINANTS OF ERROR IN DOCTORS' PROGNOSES IN TERMINALLY ILL PATIENTS: PROSPECTIVE COHORT STUDY

(Christakis NA et al, BMJ 2000; 320: 469-473)

343 doctors' survival estimates for 468 terminally ill patients at hospice referral time

Median survival 24 days

	N°	%
Accurate predictions (± 33 AS)	92	20
Overoptimistic	295	63
Over pessimistic	81	17

Overstimated survival by a factor of 5.3

Non-oncology medical specialists were 326% more likely than general internists to make overpessimistic predictions. As duration of doctor-patient relationship increased and time since last contact decreased, prognostic accuracy decreased.

The SUPPORT Prognostic Model: Objective Estimates of Survival for Seriously Ill Hospitalized Adults

(Knaus W, Ann Intern Med, 1995)

- **Comparison of the Various Models for Prediction of 180-Day Survival***

Disease class	SUPPORT Model	SUPPORT Model with APS†	Physician's Estimate	SUPPORT Model and Physician's Estimate
All (n = 4028, deaths = 1899)	0.78	0.78	0.78	0.82
Acute respiratory failure and multiple organ system failure (n = 2057, deaths = 993)	0.77	0.78	0.78	0.82
Chronic obstructive pulmonary disease congestive heart failure, cirrhosis (n = 1111, deaths = 346)	0.71	0.70	0.70	0.75
Coma (n = 281, deaths = 205)	0.74	0.75	0.78	0.82
Colon and lung cancer (n = 579, deaths = 345)	0.78	0.70	0.77	0.82

* All calculations are based on 4028 SUPPORT phase II patients who completed 180 days of follow-up and had a physicians' prognostic estimate at study day 3. Each statistic is the area under the receiver-operating characteristic curve for 180-day vital status.

† APS = APACHE III acute physiology score.

IMPROVED ACCURACY OF PHYSICIANS' SURVIVAL PREDICTION FOR TERMINALLY ILL CANCER PATIENTS USING THE PALLIATIVE PROGNOSTIC INDEX

(Morita T, Palliat Med, 2001)

Two sequential prospective studies on two independent series(n=150-108)

	1 st	2nd	p
Cases with differences between AS and CPS $\geq$ 28 days	42%	23%	$<$.01
Cases with AS twice longer or half shorter than CPS	49%	37%	=.05
Serious errors (AS 28 days and twice longer or 28 days and half shorter than CPS)	27%	16%	=.028

A systematic review of physicians' survival predictions in terminally ill cancer patients

(Glare, BMJ, 2003)

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.

Translating clinical research into clinical practice: impact of using Prediction Rules to make decisions

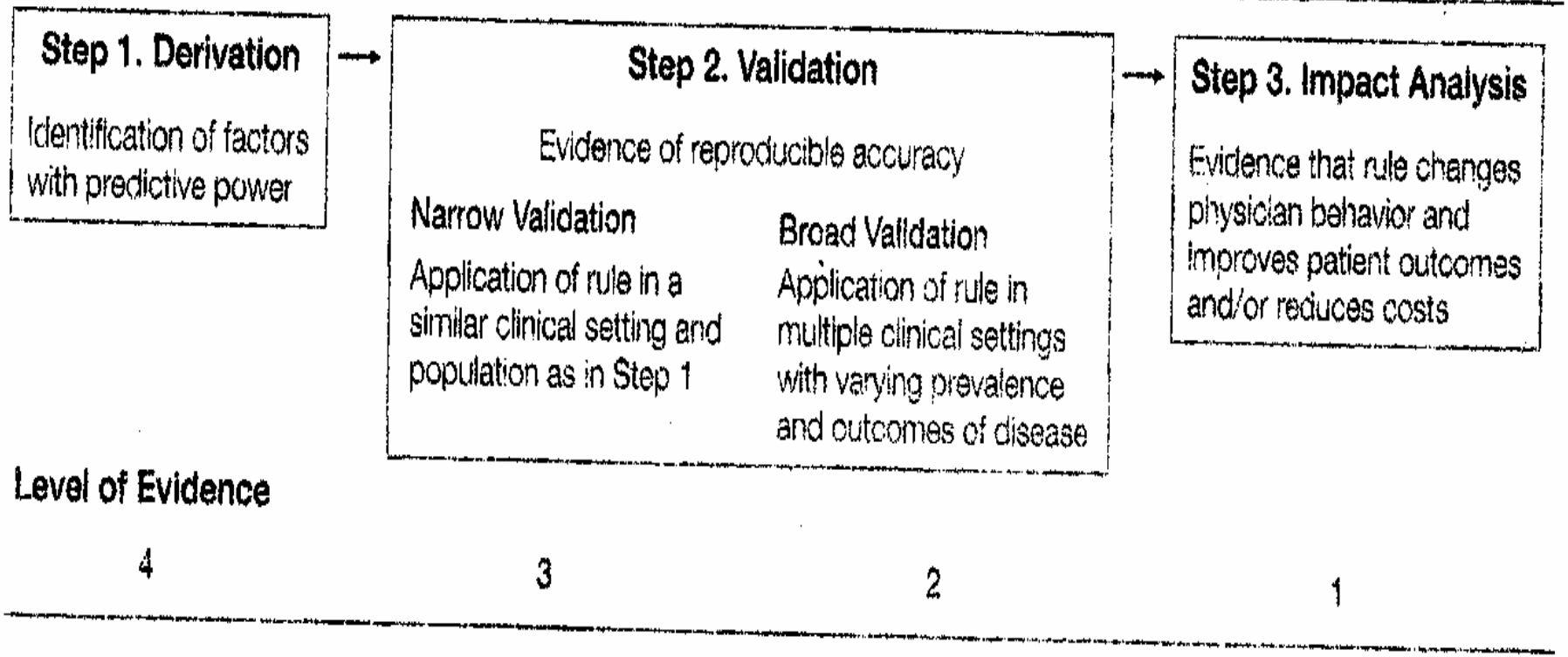
(Reilly B, Ann Intern Med, 2006)

- **Prediction rule: "suggest a diagnostic or therapeutic course of action"→ "change clinical behavior and reduce unnecessary costs while maintaining quality of care and patient satisfaction": decision rule**

Users' guide to the medical literature XXII: how to use articles about Clinical Decision Rules

(Mc Ginn T, JAMA, 2000)

Figure 2. Development of a Clinical Decision Rule



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- **Use of CDRs is warranted only if they change physician behavior and if that behavior change results in improved patient outcomes or reduced costs while maintainig quality of care**

- **Obstacles: -clinicians' intuitive estimation of probabilities may be as good as, if not better than, the CDR; -calculations involved may be cumbersome, and clinicians may, as a result, not use the CDR; -practical barriers (protecting themselves against litigation); -willingness to go on with chemo ("inertial oncology")**

SUPPORT Principal Investigators. A controlled trial to improve care for seriously ill hospitalized patients. The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment

(JAMA,1995, 274:1591)

- **Controlled clinical trial, 9000 pts**
- **In the interventional arm, doctors provided with: - informations on prognosis; -patients'preferences; - a trained nurse to facilitate communication**
- **No impact on: -doctor-patient communication or understanding by the doctor of the patient's wishes;**

  - changes in the timing of signing the DNR order;

  -pain reduction; -reduction in the number of days spent in an undesidered care setting; -reduction in the inappropriate use of hospital resources.

UNDERSTANDING OF PROGNOSIS AMONG PARENTS OF CHILDREN WHO DIED OF CANCER. IMPACT ON TREATMENT GOALS AND INTEGRATION TO PALLIATIVE CARE

(Wolfe, JAMA, 2000)

103 parents of children with cancer

Recognition of no realistic chance for cure before child's death

parents: 106 days (150 SD)

doctors: 206 days (330 SD)

Earlier vs late recognition (cut-off: 50 days)

- earlier discussion of hospice care (OR, 1.03; p=.01)
- better parental ratings of the quality of home care (OR,3.31; p=.03)
- earlier institution of a DNR order (OR, 1.03; p=.02)
- higher likelihood of the correct perception of cancer-directed therapy goal (OR, 5.17; p=.002 doctors) (OR, 6.56; P=.01 parents)

- LESS USE OF CANCER-DIRECTED THERAPY IN THE LAST MONTH OF LIFE (OR, 2.8; p=.04)

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PaP Score groups according to their 30-day survival probability estimate

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OBJECTIVES

- **Evaluation of the PaP Score in a patient population different from the one it was constructed**
- **Validation of the predictive capacity of the PaP Score in a setting of advanced cancer patients who are candidates for palliative chemotherapy**

ELIGIBILITY CRITERIA

- **INCLUSION CRITERIA:**
  - **Patients with histological diagnosis of non small cell lung cancer or gastrointestinal tumours**
  - **Patients with metastatic visceral or bone disease**
  - **Patients who are candidates for second- or third-line palliative chemotherapy in progression after previous chemotherapy**
- **EXCLUSION CRITERIA:**
  - **Patients undergoing locoregional treatment**
  - **Patients with haematological disease**
  - **Patients with cerebral metastases**

Demographic and clinical characteristics of the 173 patients

Table 1. Demographic and clinical characteristics of the patients.

Characteristic	Value
Number of patients	173
Age (years)	
• Median	63
• Range	37-83
Gender	
• Male (%)	113 (65)
• Female (%)	60 (35)
Primary tumor sites	
• Colorectal Cancer (%)	95 (53)
• Non Small Cell Lung Cancer (%)	60 (35)
• Gastric Cancer (%)	12 (7)
• Pancreatic, Hepatic or Biliary Tract Cancer (%)	10 (5)
Number of metastatic sites	
• One (%)	53 (31)
• Two (%)	96 (56)
• More than two sites (%)	19 (11)
Previous chemotherapy lines	
• One line (%)	101 (58)
• Two lines (%)	57 (33)
• More than two lines (%)	15 (9)
Concomitant symptomatic treatments	
• Steroids (%)	79 (45.6)
• NSAIDs (%)	50 (28.9)
• Anabolic Steroids (%)	11 (6.3)
• Opiates (%)	40 (23.1)

Table 2. PaP-Score items in the patients.

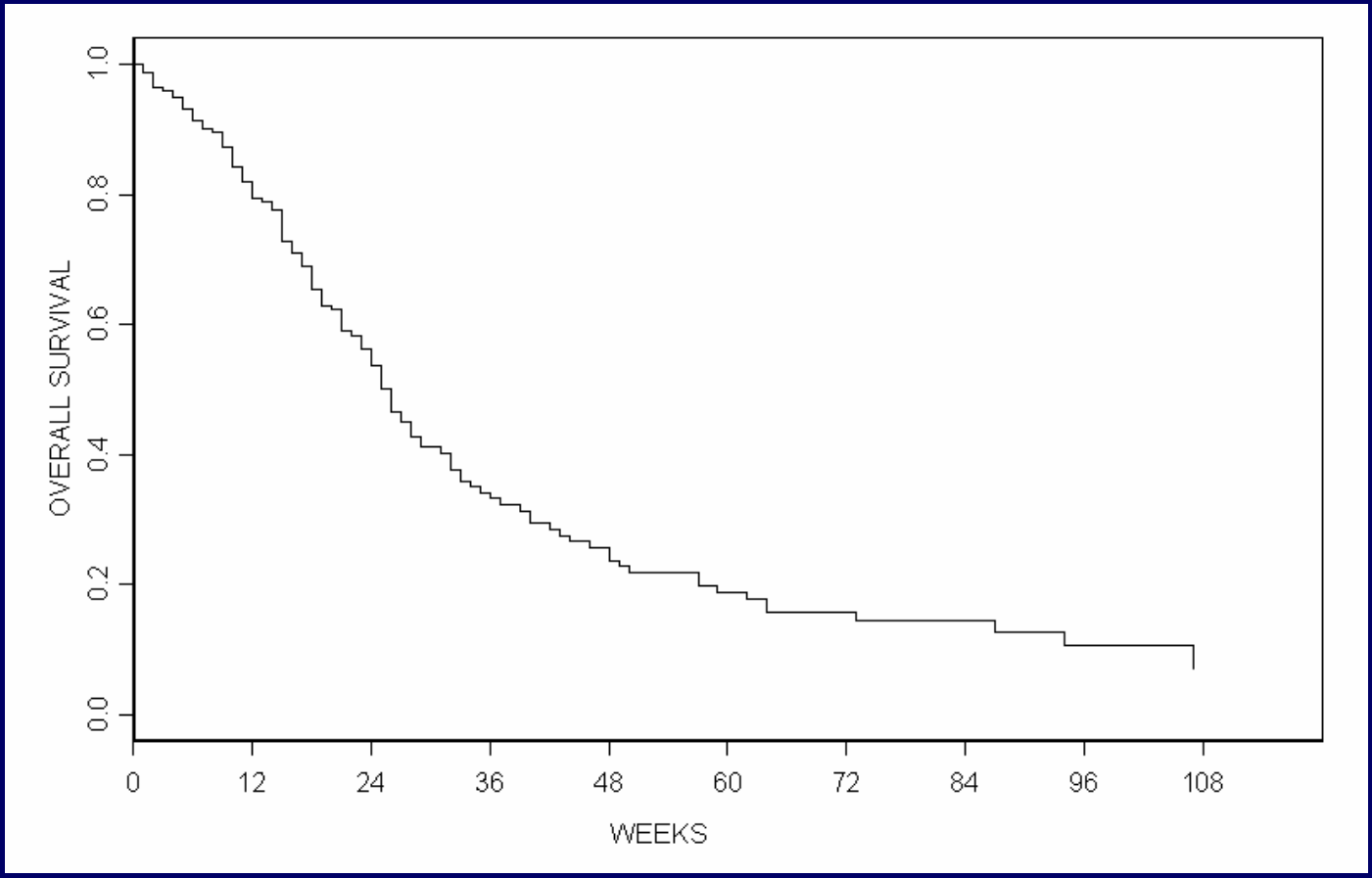
Item	Value	Percentage
Symptoms		
• Anorexia	34	20
• Dyspnea	53	31
Karnofsky Performance Status		
• ≥50	165	95
• 30-40	8	5%
• 10-20	0	0
Clinical Prediction of Survival (weeks)		
• >12	141	81.5
• 11-12	17	16
• 9-10	1	0.5
• 7-8	1	0.5
• 5-6	3	1.5
• 3-4	0	0
• 1-2	0	0
Total White Blood Cells		
• Normal (4800-8500/mm^3)	101	58
• High (8501-10000/mm^3)	41	24
• Very high (>11000/mm^3)	31	18
Lymphocyte Percentage		
• Normal (20%-40%)	101	58
• Low (12%-19%)	41	24
• Very low (≤11.9%)	31	18
PaP-Score Groups		
• A	150	87
• B	23	13
• C	0	0

SURVIVAL

- **Patients: 173 (100%)**
- **Median OS: 23 weeks**
- **30-day OS: 95%**

Median OS

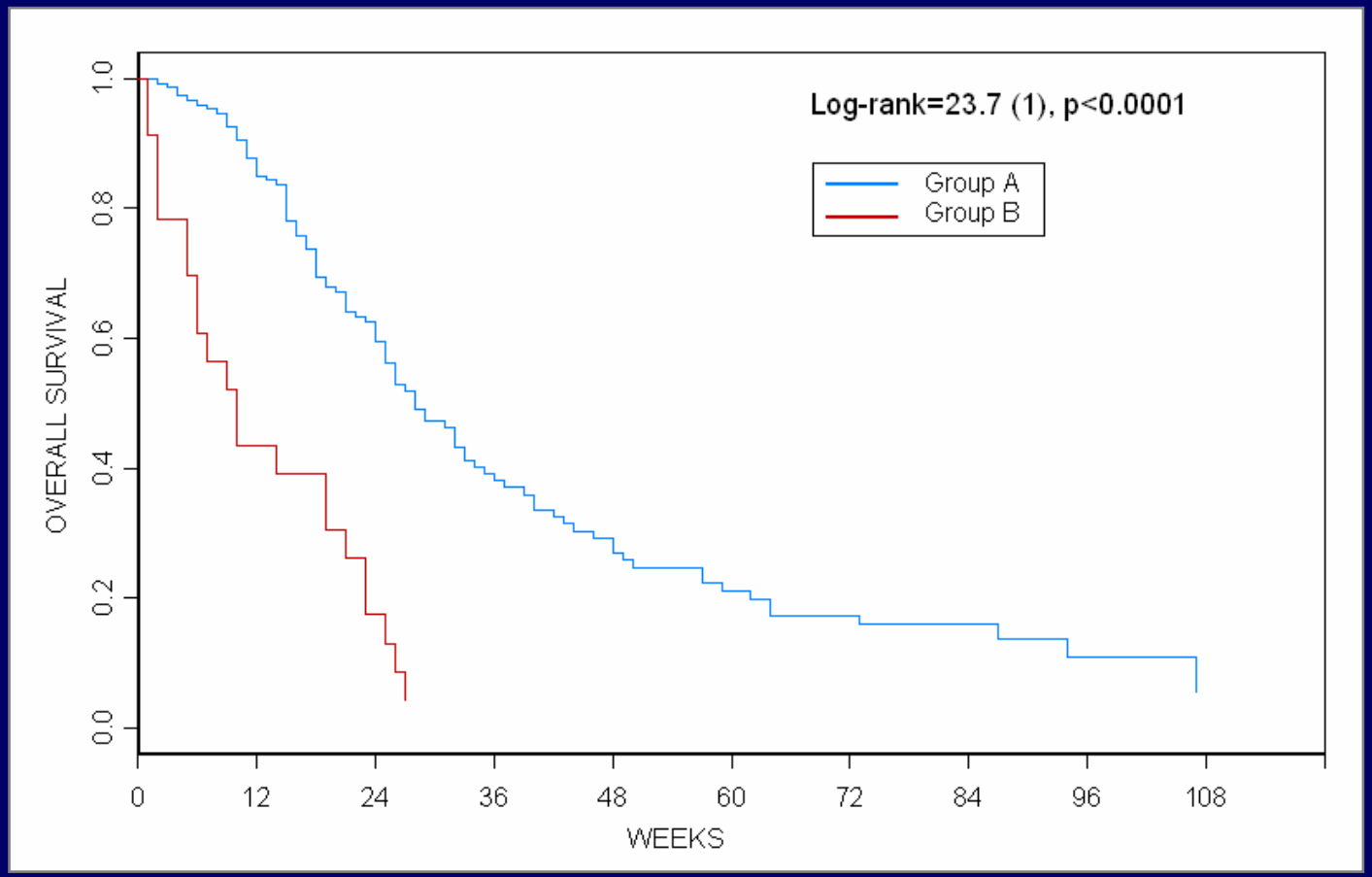
• Training set	32 days
• Testing set	33 days
• This Study	161 days



SURVIVAL BY PAP SCORE

Group A :
- **Patients: 150 (87%)**
- **Median OS: 28 weeks**

Group B :
- **Patients: 23 (13%)**
- **Median OS: 10 weeks**



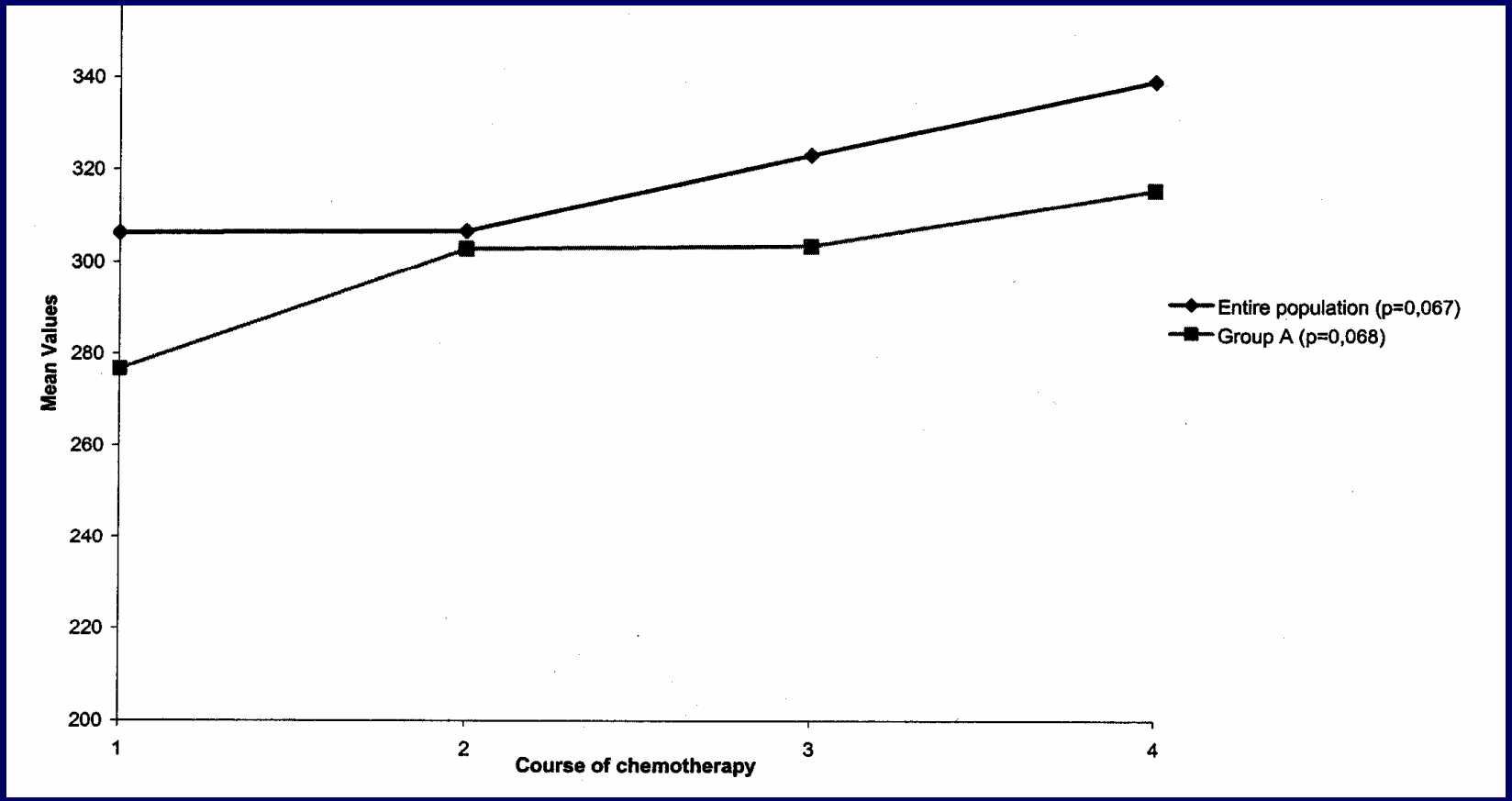
RESULTS

Cycles of chemotherapy	Group A	Group B	Total	
			No	%
1	150 (100)	23 (100)	173	100
2	129 (86)	12 (52)	141	82
3	106 (70)	8 (28)	114	66
4	69 (46)	4 (17)	73	42
5	54 (36)	3 (13)	57	33
6	45 (30)	1 (4)	46	27

Validation of the PaP Score in different population settings

	Training set 519 pts; ms 32 days			Testing set 502 pts; ms 33 days			Chemo set 173 pts; ms 161 days		
Risk group	(%)	30day s (%)	Median s (days)	(%)	30day s (%)	Median s (days)	(%)	30day s (%)	Median s (days)
A	34.3	82.0	64	28.2	86.6	76	87	78	175
B	39.5	52.7	32	45.7	51.6	32	13	82.6	62
C	26.2	9.6	11	26.1	16.8	14	\	\	\

Trend in symptom assessment using the ESAS Scale



CONCLUSIONS

- **The PaP Score demostrated its capacity to identify two different prognosis groups in a setting of patients who are candidates for palliative chemotherapy**
- **The PaP Score could be used in clinical practice to select the most suitable treatment strategy**
- **Group B Pap Score patients should be carefully evaluated before being initiated to a palliative chemotherapy program**

A possible next step for research

- **Difference in survival in Palliative Care Setting and Chemo setting due to chemo or to different inherent conditions?**
- **Next step: same setting, identify one Group (B) or both (B and A) and randomize pts in each group to chemo or BPC: if no difference in survival, and worsening in QoL from chemo, you could (should?!) choose BPC**

Probabilistic value of prognostic factors

“The prognosis of any individual shall always be either better or worse than the median of a group of patients at the same stage of the same disease”

Selawry, The individual and the median, 1979