

# Elderly and PS 2 Patients

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# Disclosures

- None for this presentation

# PS2 patients with NSCLC

## What we (don't) know

1. Heterogeneous group of patients
2. 30%–40% of the NSCLC population
3. Frequently excluded from clinical trials
  - When included, lumped with the elderly, although each represents different populations
4. Generally tolerate therapy poorly
5. Associated with poorer survival

# PS2 patients with NSCLC

## What we (don't) know

1. How to accurately assess PS2 patients
2. The influence of co-morbidities vs disease burden on PS and treatment outcome
3. Best therapy

# Performance status 2

- **PS 2**

Ambulatory and capable of all selfcare but unable to carry out any work activities.  
Up and about more than 50% of waking hours

- **PS 3**

Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours

# Assessment of performance status

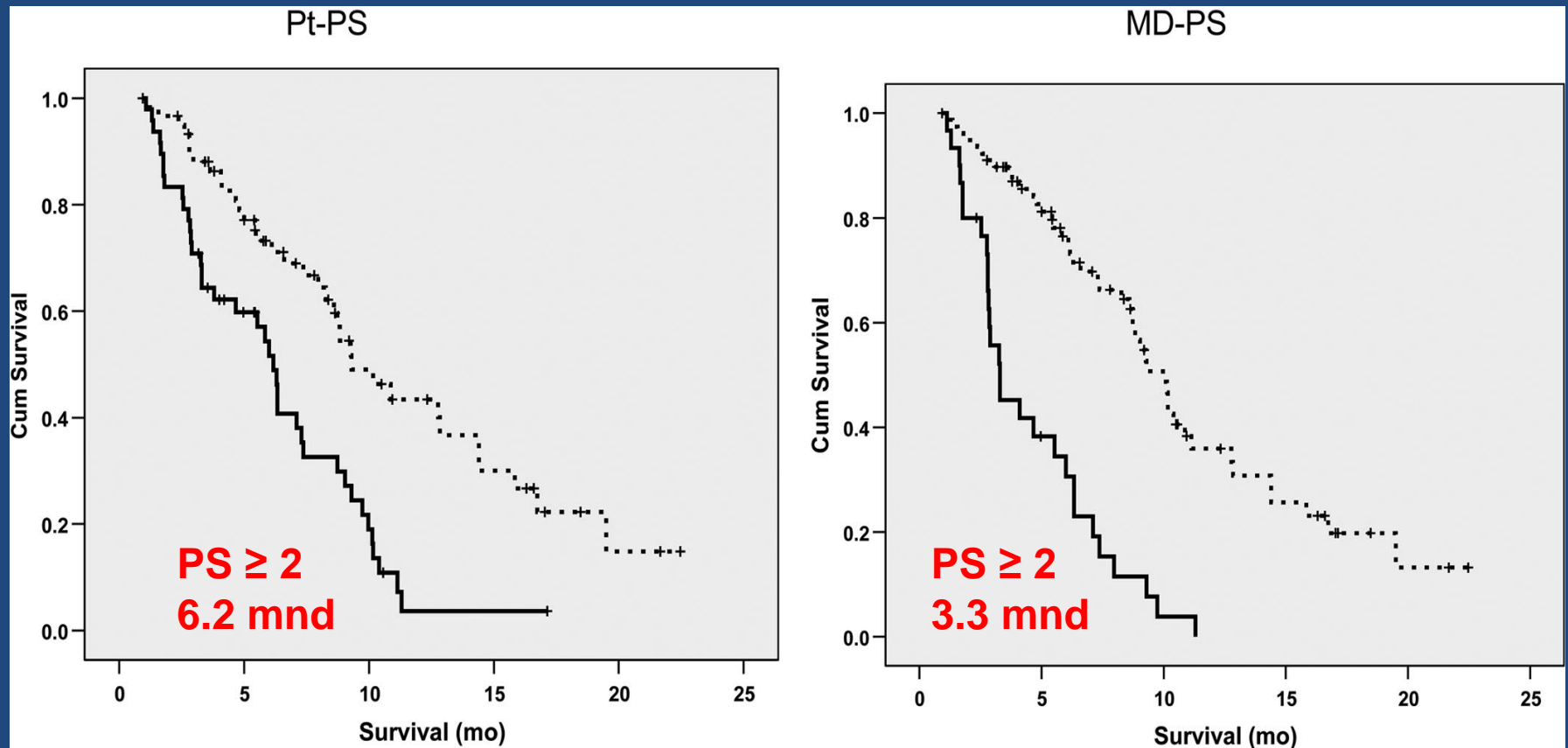
**TABLE 2.** Patient-Rated and Provider-Rated ECOG PS, Lung Cancer Patients (n = 503)<sup>a</sup>

Patient-Reported ECOG PS	Provider-Reported ECOG PS					Total	
	0	1	2	3	4		
0	59	38	6	4	0	107	(22.0)
1	43	77	21	2	0	146	(30.0)
2	16	69	53	20	2	163	(33.5)
3	2	19	25	22	1	70	(14.4)
4	0	3	1	7	3	15	(3.1)
Total	121 (24.4)	207 (41.8)	106 (21.4)	55 (11.1)	6 (1.2)		

All values inside parentheses indicate percentages.

<sup>a</sup> Eight patients were missing patient-rated PS, two patients were missing provider rated PS.  
ECOG PS, Eastern Cooperative Oncology Group Performance Status.

# Assessment of performance status



# Conclusion

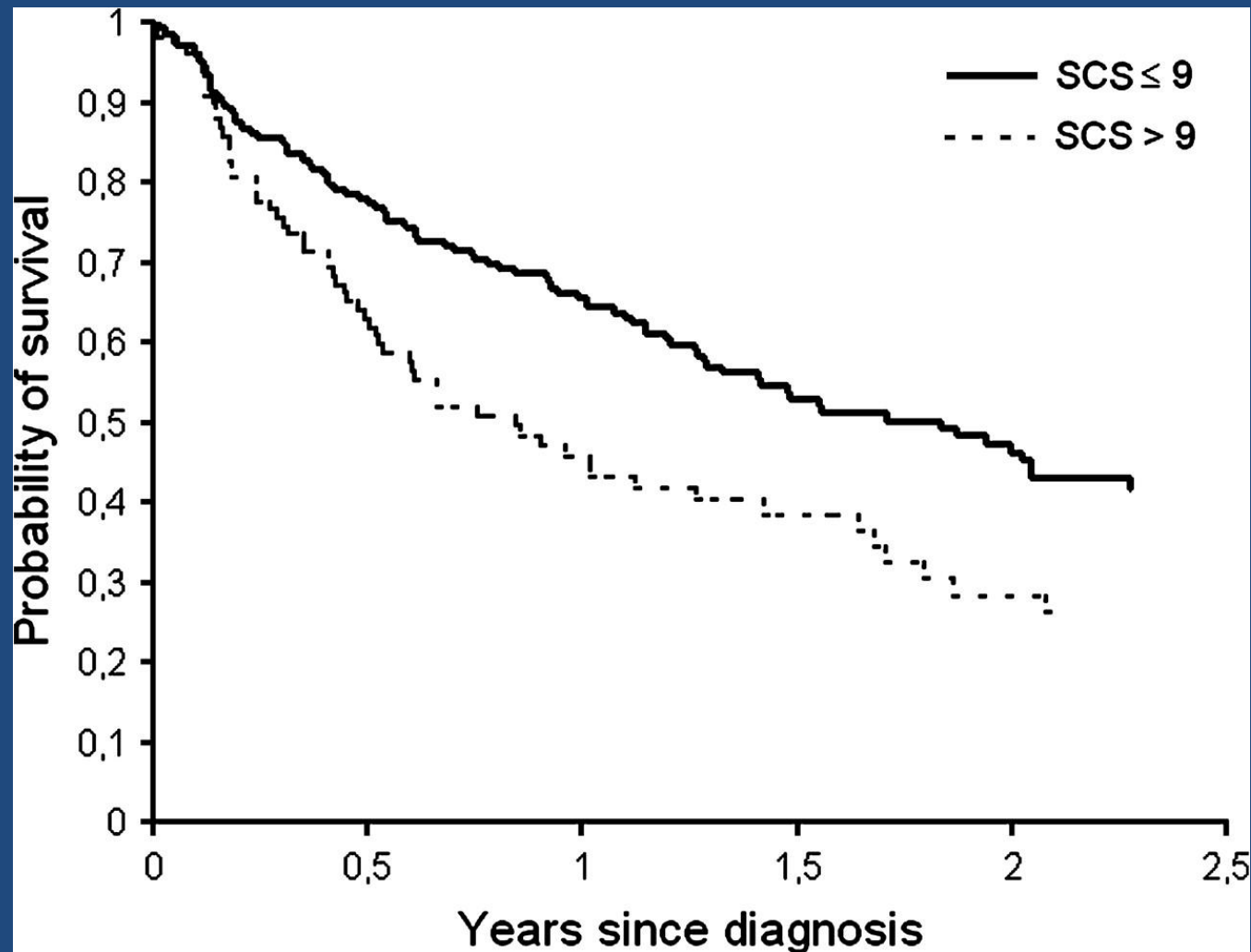
- Doctors and other health care providers are too optimistic when assessing PS.
- Need for accurate PS assessment tools.



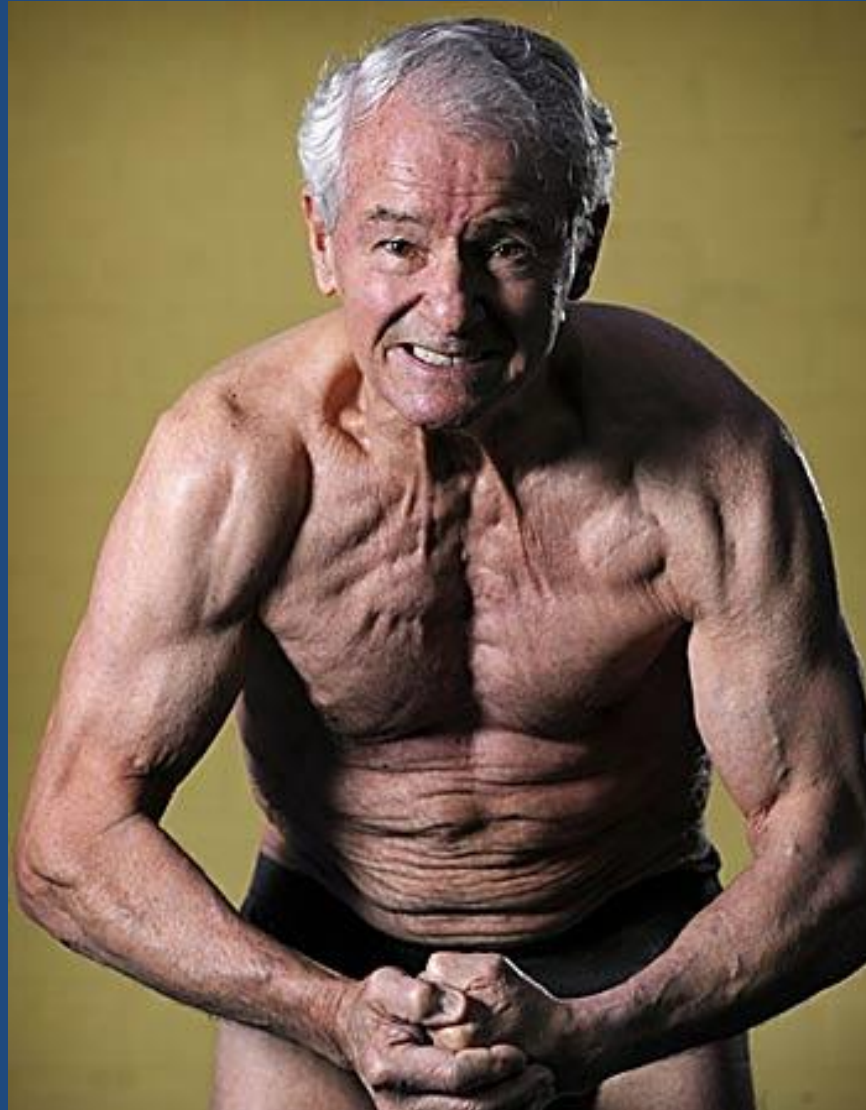
# Comorbidity

		% with co-morbidity	
Age	N	Male	Female
<45	4898	9	12
45-59	12089	32	24
60-74	22648	55	47
>75	13475	62	59

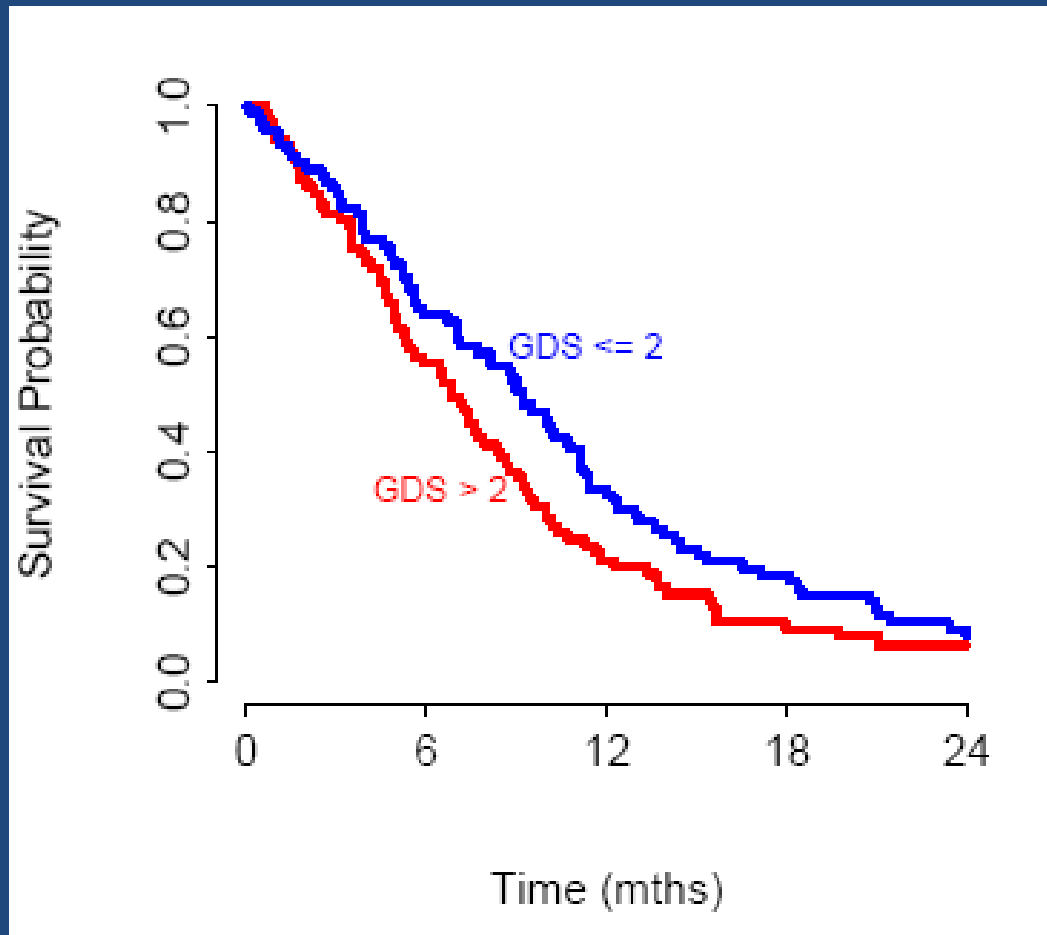
# Survival according to comorbidity



Comorbidity may go unnoticed



# And includes psychological factors



# Impact of PS on outcome

## European observational study

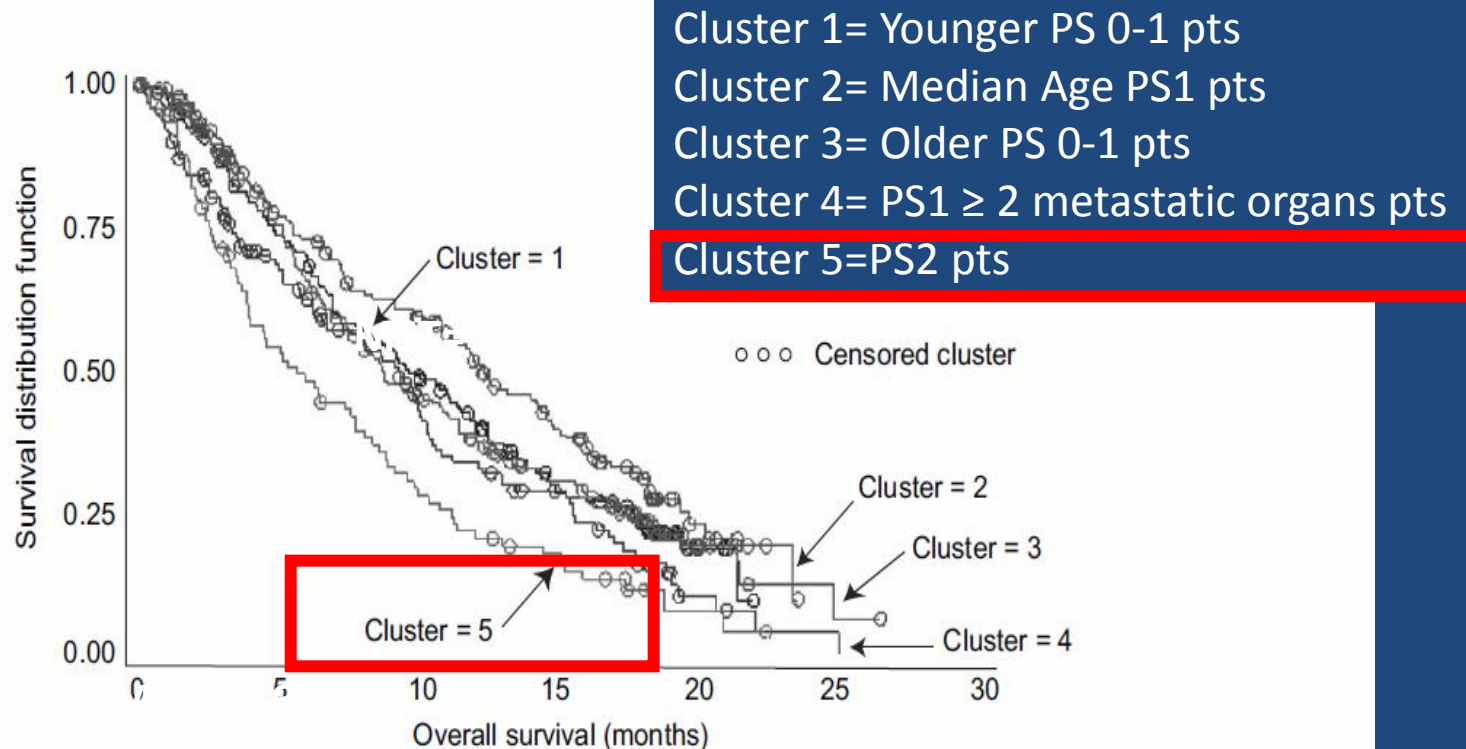


Figure 3. Unadjusted Kaplan–Meier estimates of survival (cluster analysis).

# Evolution of chemotherapy for PS2 advanced NSCLC patients

Prognostic Factor	Level of Factor	No. of Patients (%) Treated With				
		CAMP (n = 115)	MVP (n = 121)	VDA-P (n = 126)	VP-P (n = 124)	Total (n = 486)
Cell type	Squamous	43 (37)	47 (39)	50 (40)	48 (39)	188 (39)
	Adenocarcinoma	47 (42)	52 (43)	54 (42)	54 (44)	207 (43)
	Large-cell anaplastic	21 (18)	19 (16)	19 (15)	19 (15)	78 (16)
	Other	4 (3)	3 (2)	3 (2)	3 (2)	13 (3)
Initial performance status	0	20 (17)	21 (17)	22 (18)	27 (21)	90 (19)
	1	74 (64)	78 (65)	76 (60)	76 (61)	304 (63)
	2	21 (18)	22 (18)	28 (22)	21 (17)	92 (19)

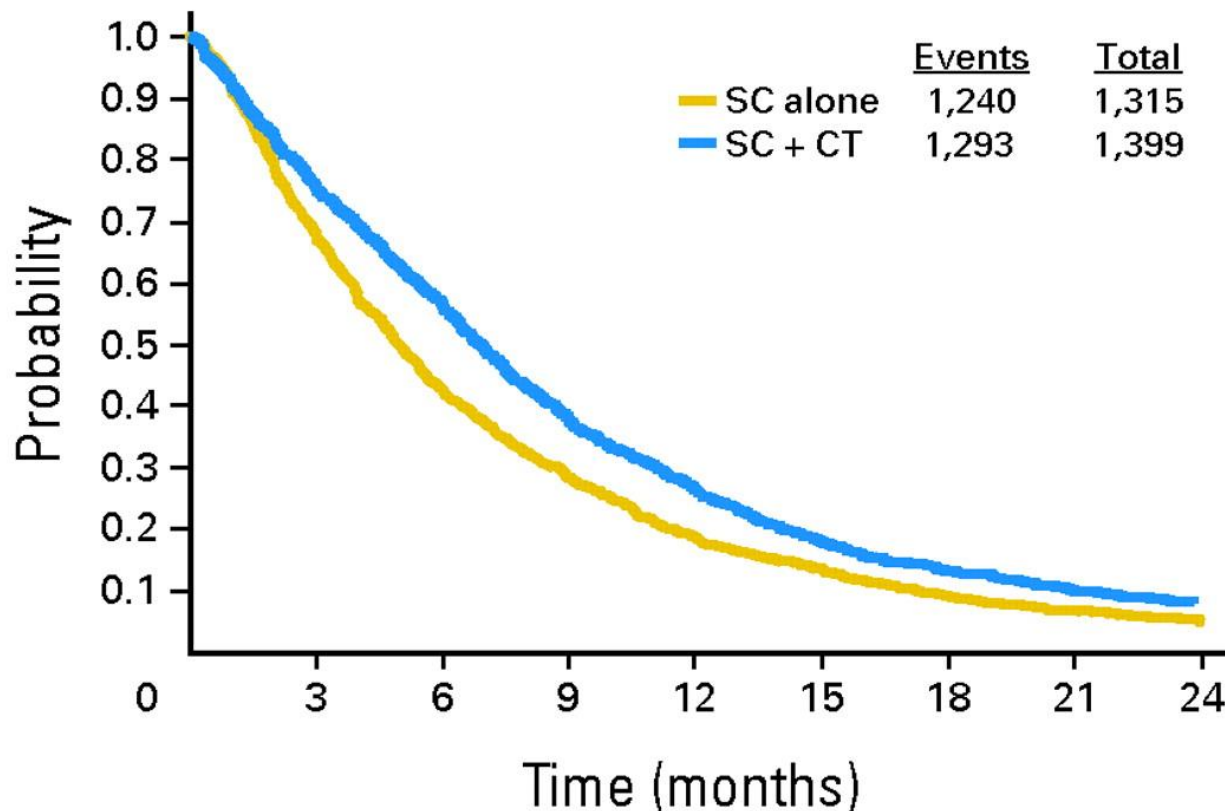
Initial performance status	0	90	26	36.0
	1	304	25	25.9
	2	92	20	10.4

Initially PS2 are not appropriate candidates for trials of new agents or combinations

# Evolution of chemotherapy for PS2 advanced NSCLC patients

- Single-agent chemotherapy SOC
  - ASCO guidelines, update 2003  
(J Clin Oncol 22:330-53, 2004)
  - European Experts Panel  
(Ann Oncol 15:419-26, 2004)

# Meta-analysis update: Chemotherapy vs BSC

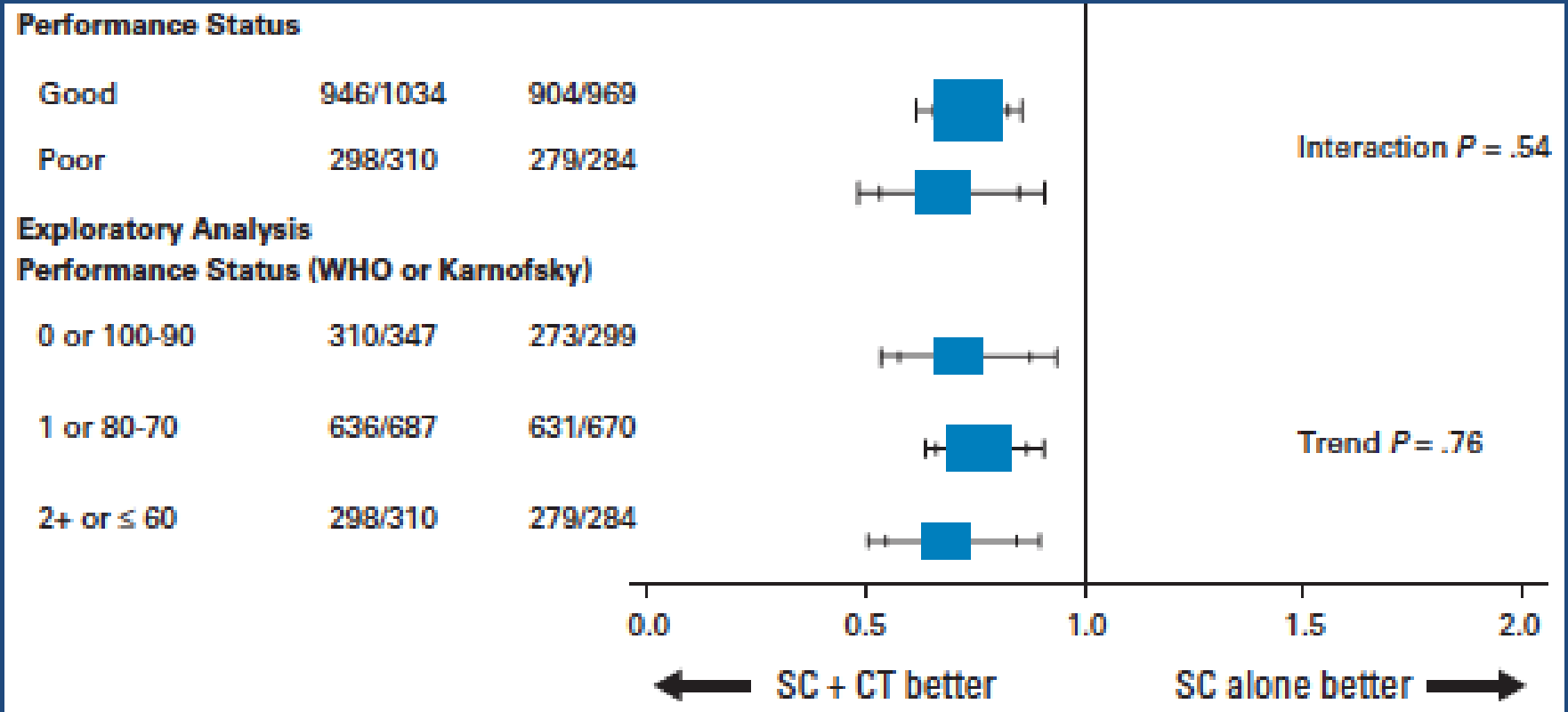


Patients at risk

SC alone	1,315	884	552	363	231	161	107	77	55
SC + CT	1,399	1,052	779	519	349	233	165	115	91



# Analysis by PS



Furthermore, despite the difference in underlying survival by PS, the absolute effect at 12 months was similar (8% vs 6%)

# Evolution of chemotherapy for PS2 advanced NSCLC patients – STELLAR 3

Chemotherapy-naïve PS2 patients with advanced NSCLC

## Stratified by:

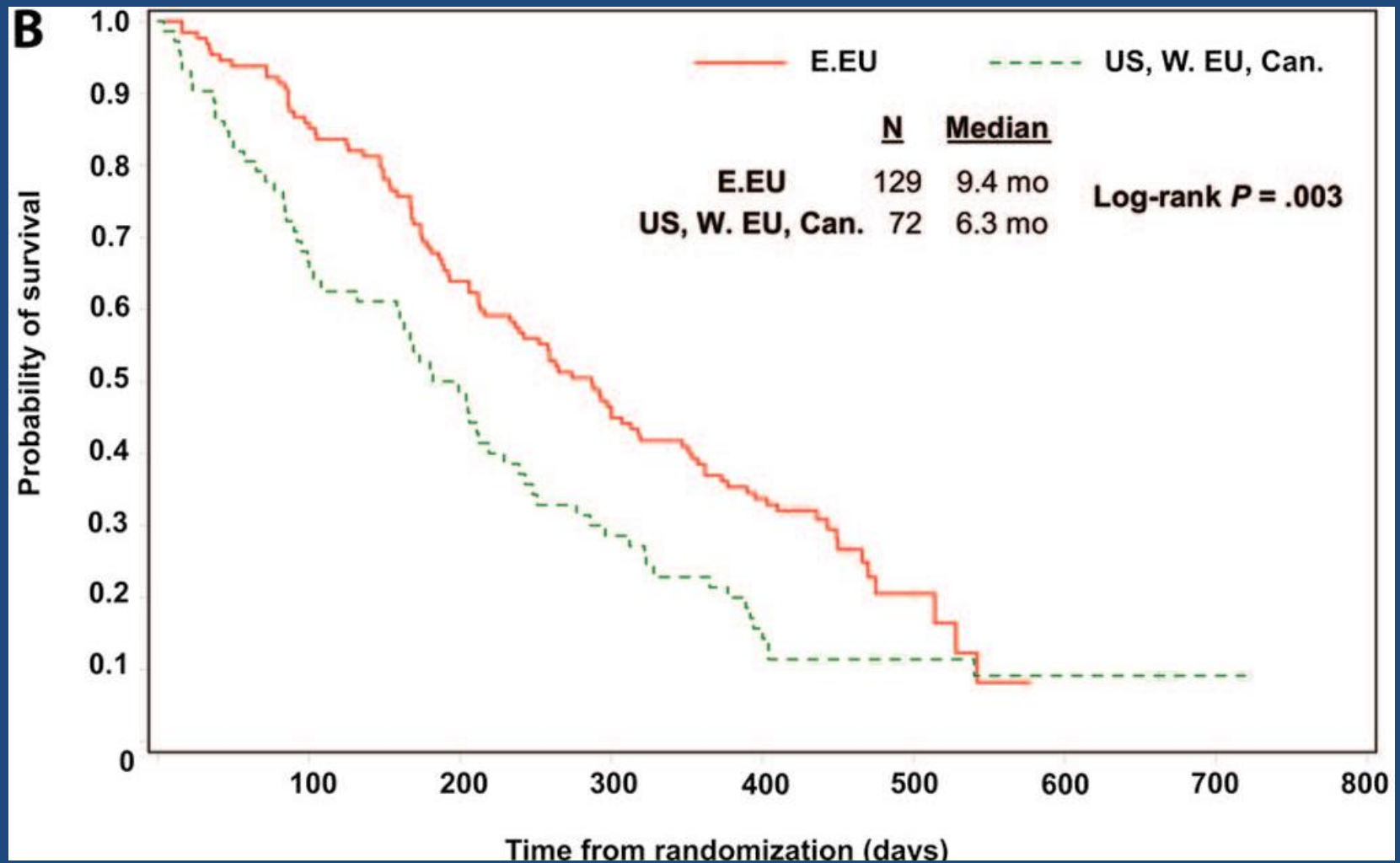
- Stage
- Sex
- History of brain mets
- Geographic region

**R  
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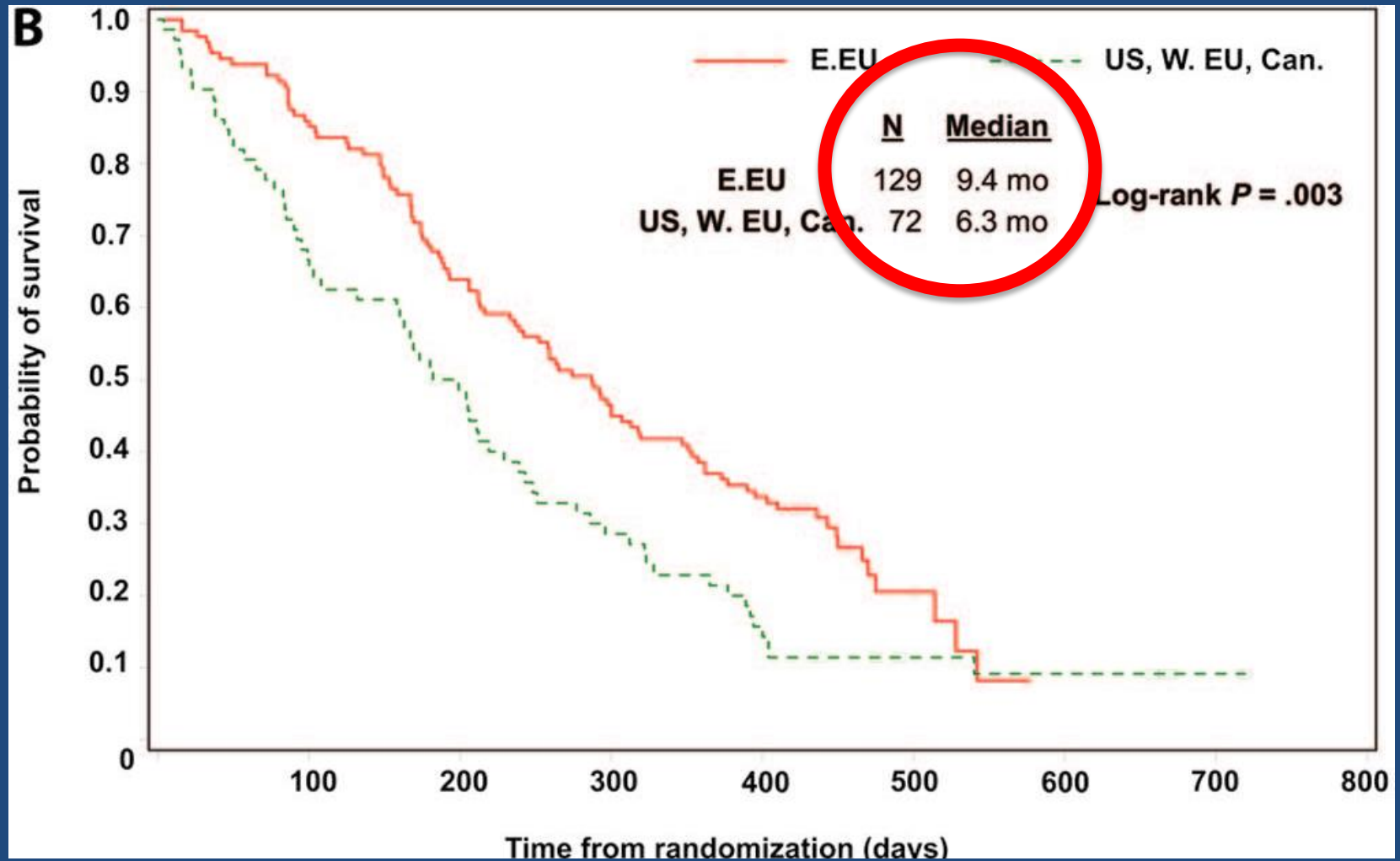
PPX 210 mg/m<sup>2</sup>  
Carboplatin (AUC 6)  
q3w  
N = 199

Paclitaxel 225 mg/m<sup>2</sup>  
Carboplatin (AUC 6)  
q3w  
N=201

# STELLAR 3 – Overall Survival



# STELLAR 3 – Overall Survival



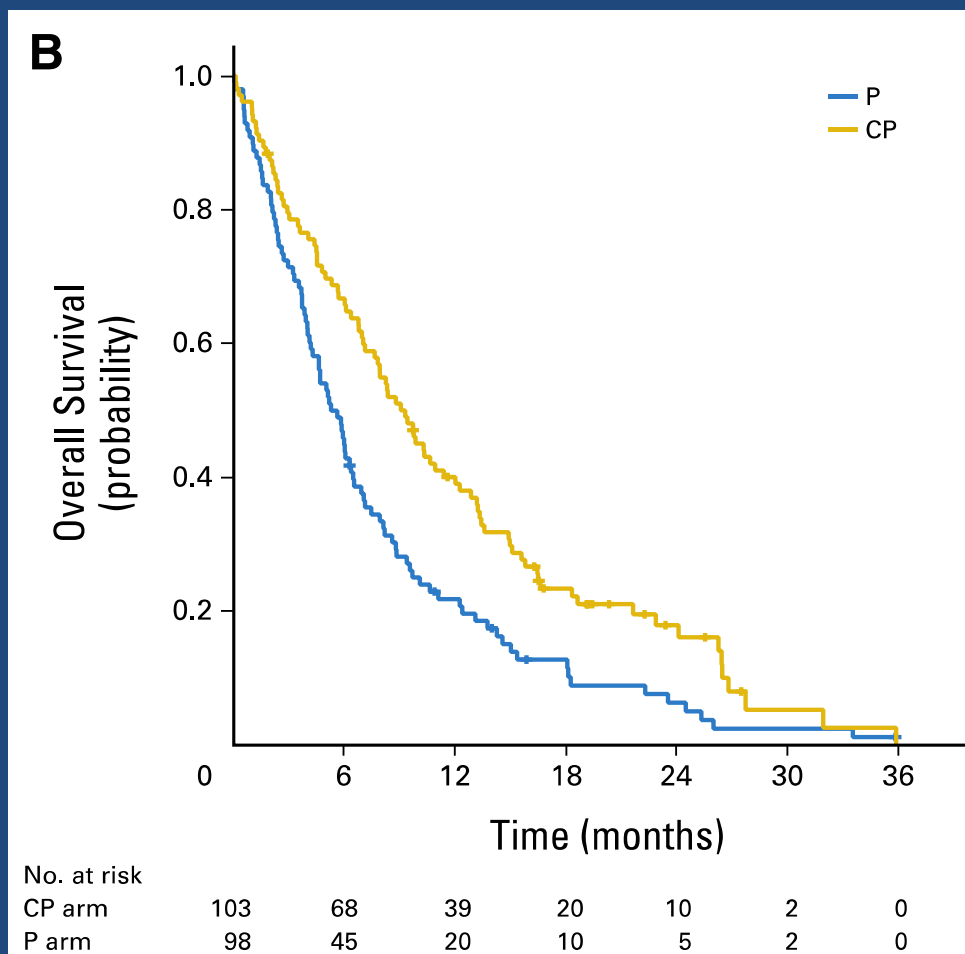
# Evolution of chemotherapy for PS2 advanced NSCLC patients

- Randomized phase III trial of single-agent pemetrexed versus carboplatin and pemetrexed
  - - April 2008-July 2011
  - 205 patients
  - 14 pts squamous cell ca
  - Primary endpoint: OS

# Randomised phase III of P vs PC in PS 2 patients

	P	PC	P value
RR (%)	10	24	0.019
PFS (months)	2.8	5.8	<0.001
OS (months)	5.3	9.3	=0.001

# Randomised phase III of P vs PC in PS 2 patients



# Randomised phase III of P vs PC in PS 2 patients

**Table 3.** Toxicity

Grade 3 or 4 Toxicity	P (n = 102)		CP (n = 103)		<i>P</i>
	No.	%	No.	%	
Anemia	4	3.9	12	11.7	.07*
Thrombocytopenia	0	0.0	1	1.0	1.00*
Neutropenia	1	1.0	7	6.8	.06*
Febrile neutropenia	3	2.9	1	1.0	.37*
Nausea/emesis	1	1.0	5	4.9	.21*
Diarrhea	2	2.0	1	1.0	.62*
Dyspnea	11	10.8	6	5.8	.19†
Grade 5 event‡	0	0.0	4	3.9	.12*

Abbreviations: CP, combination of carboplatin and pemetrexed;  
P, pemetrexed

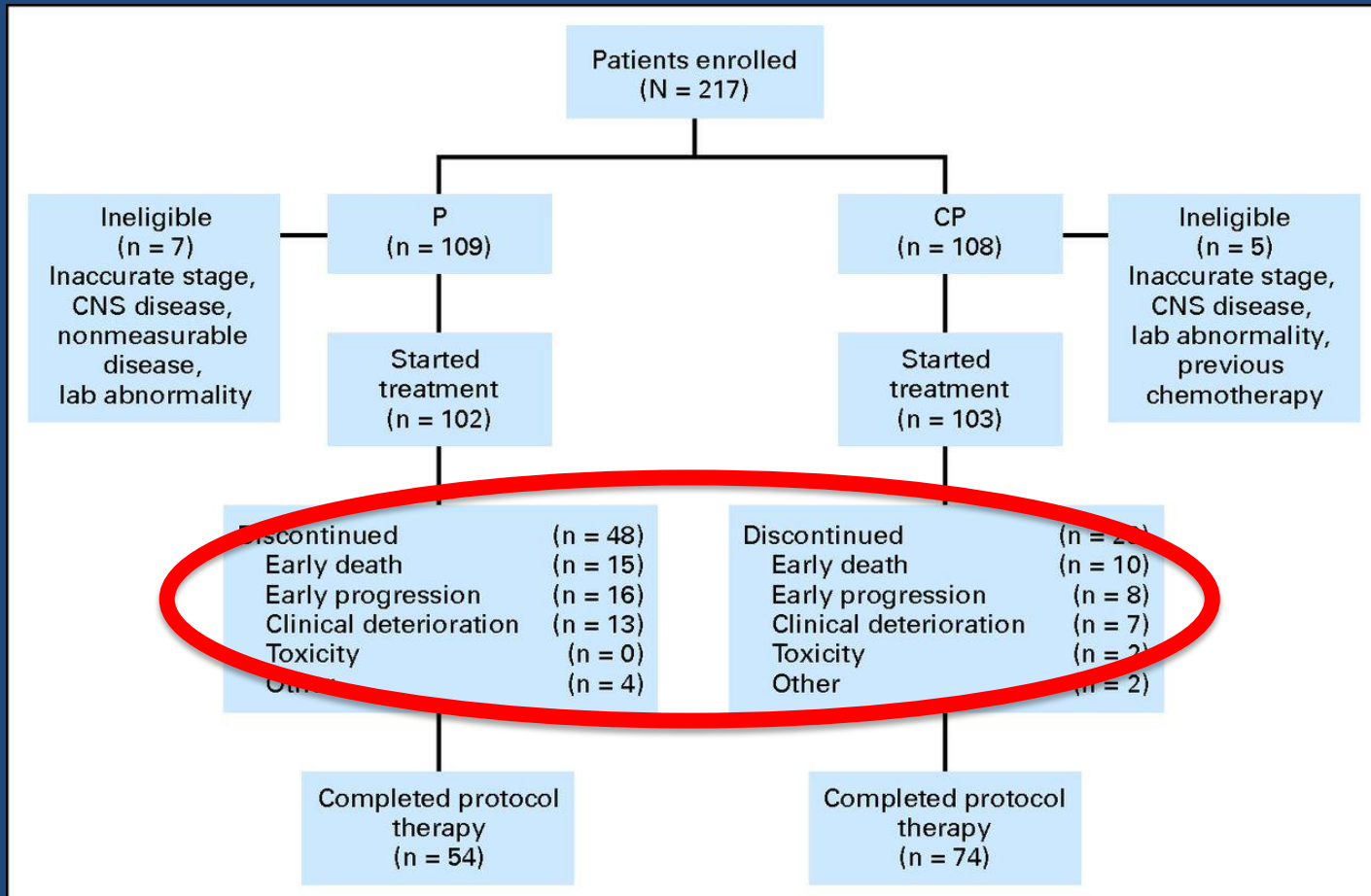
\*Fisher's exact test.

† $\chi^2$  test.

‡Renal failure, sepsis, pneumonia, and thrombocytopenia.



# Randomised phase III of P vs PC in PS 2 patients



# PS 2 and combination chemotherapy

## *ASCO update 2012*

”Findings represent a paradigm shift in the standard of care for PS 2 patients with advanced NSCLC, underscoring the importance of not undertreating this patient population”

# Combination chemotherapy and QoL in responders to CT

Function	PS 0-1	PS 2	P values
n= 277	improved (%)	Improved (%)	
Global QoL	32	48	<0.01
Role function	26	38	0.01
Cognitive function	26	39	<0.01
Fatigue	32	48	0.03
Pain	36	48	0.09
Dyspnea	29	54	<0.01
Appetite loss	26	40	0.02

# EGFR TKI' s in PS 2

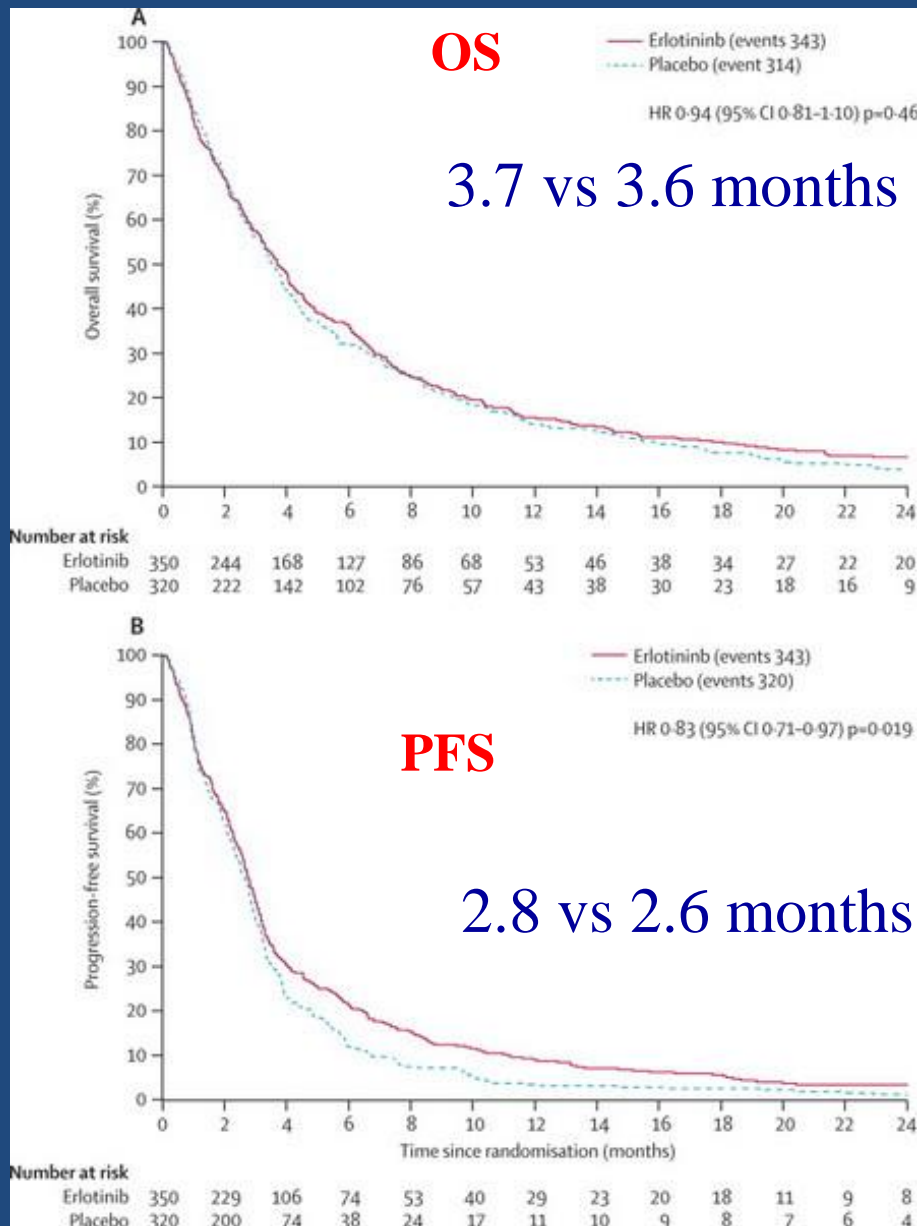


# TOPICAL

- Randomized phase III (UK)
- Erlotinib vs Placebo
- *Unselected*
- PS  $\geq 2$  and/or comorbidities ++
- 670 pts

# Topical

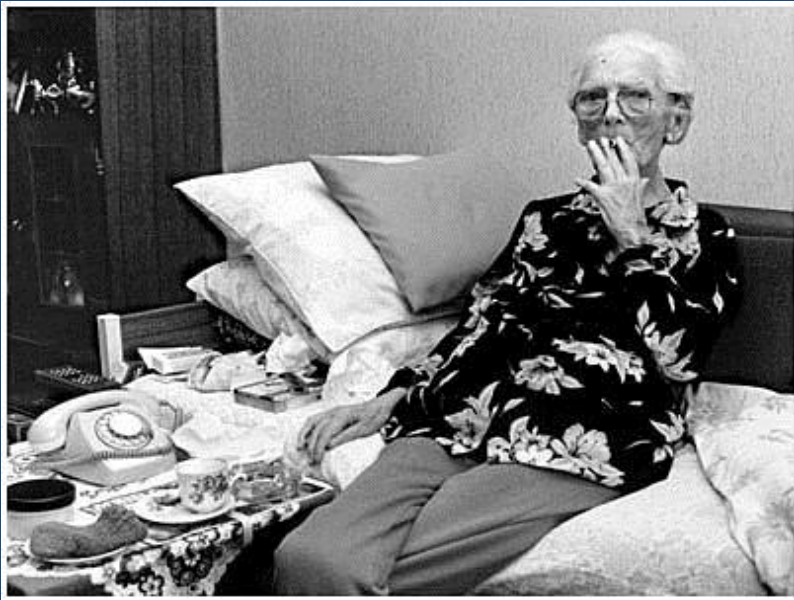
OS en PFS for all patients



# Elderly patients

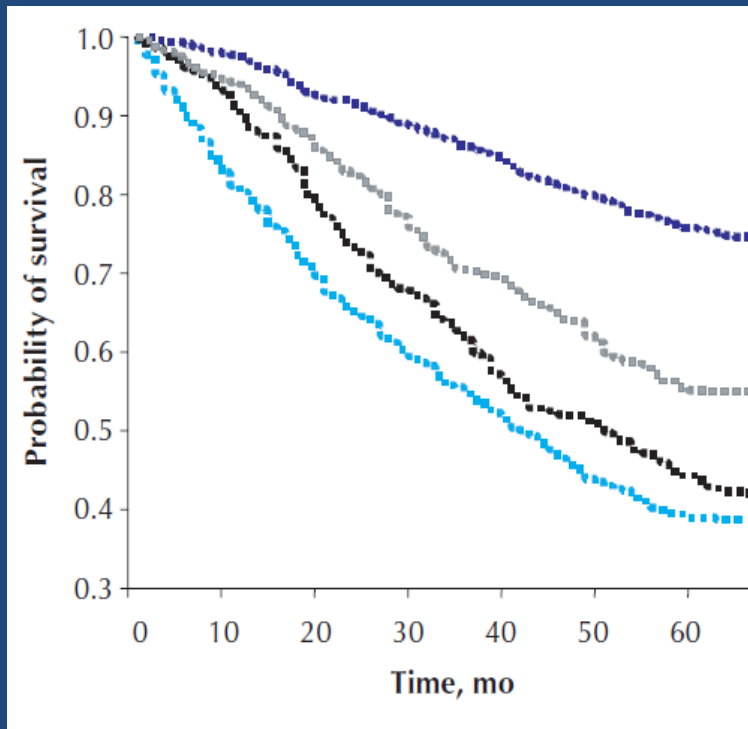
- Similar set of problems:
  1. Heterogeneous group of patients
  2. 50% of the NSCLC population
  3. Frequently excluded from clinical trials
    - When included, lumped with the PS2, although each represents different populations
  4. Generally tolerate therapy poorly
  5. Associated with poorer survival
  6. How to assess elderly patients
  7. Best therapy

# Elderly – Heterogeneous group





# Screening Tools



STANDARD THERAPY



TAILORED  
APPROACH



PALLIATIVE  
CARE

# Comprehensive Geriatric Assessment

- To improve diagnostic accuracy
- To guide selection of interventions
- To recommend an optimal environment for care
- To predict clinical outcomes
- To monitor clinical changes over time

# Comprehensive Geriatric Assessment

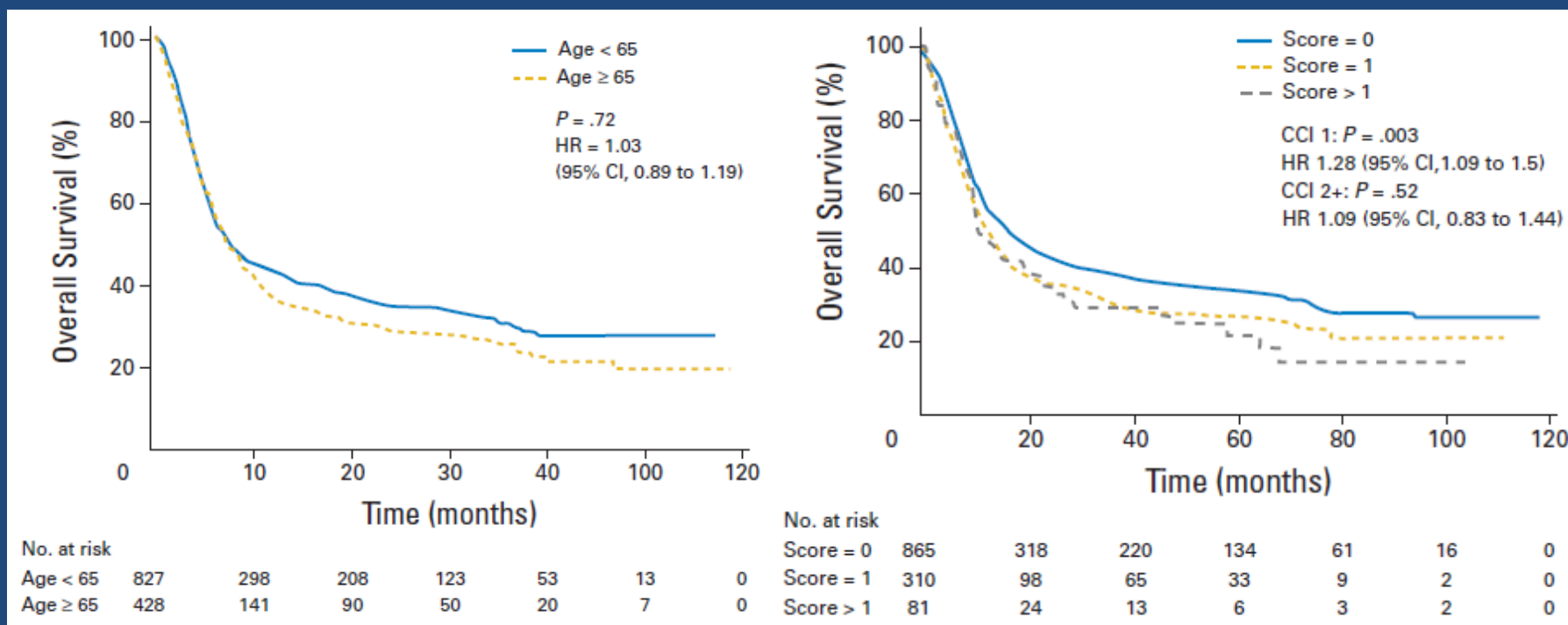
- Charlston comorbidity index
- Cumulative Illness Rating Scale – Geriatrics
- ADL
- IADL
- Timed Up and Go test
- Mini Mental State Examination
- Geriatric Depression Scale
- Positive and Negative Affect Schedule
- GFI

# Comprehensive Geriatric Assessment

- Charlston comorbidity index
- Cumulative Illness Rating Scale – Geriatrics
- ADL
- IADL
- **NOT TESTED HEAD TO HEAD**
- Mini Mental State Examination
- Geriatric Depression Scale
- Positive and Negative Affect Schedule
- GFI

# Age and Comorbidity As Independent Prognostic Factors in the Treatment of Non-Small-Cell Lung Cancer: A Review of National Cancer Institute of Canada Clinical Trials Group Trials

Timothy R. Asmis, Keyue Ding, Lesley Seymour, Frances A. Shepherd, Natasha B. Leigh, Tim L. Winton, Marlo Whitehead, Johanna N. Spaans, Barbara C. Graham, and Glenwood D. Goss

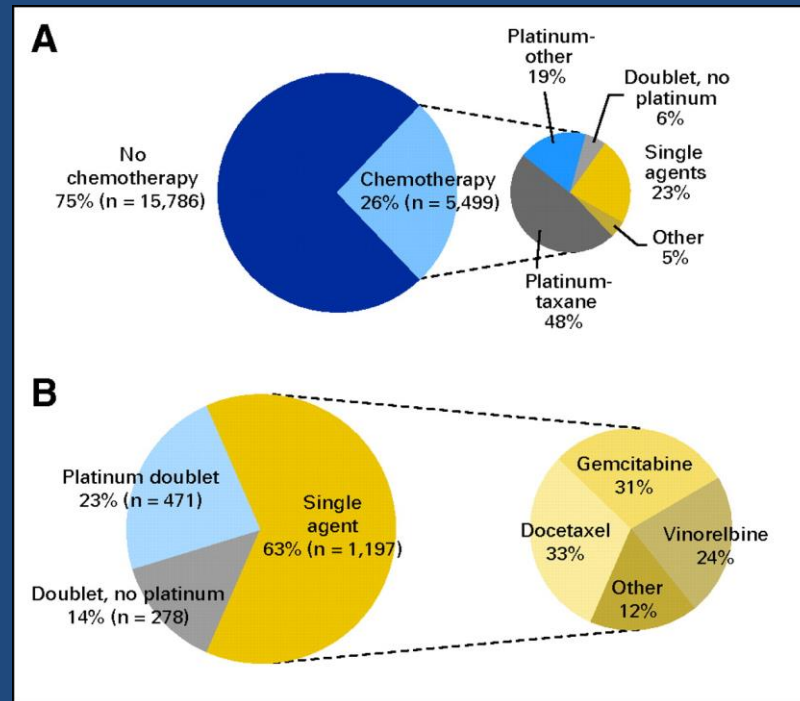


# NSCLC in the elderly: barriers to treatment

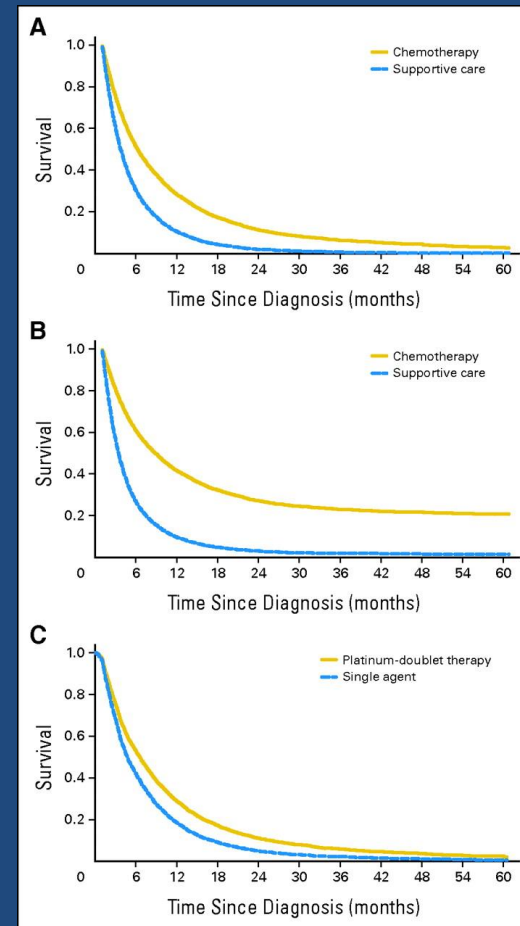
- Presence of co-morbid conditions
- Hesitation to treat and/or to treat aggressively
  - *Elderly have less aggressive cancers*
  - *Elderly do not want aggressive therapy*
  - *Elderly cannot tolerate aggressive therapy*
  - *Elderly have different wishes with respect to prolongation of life*
- Psychological (*“treatment is worse than the disease”*)
- Underrepresented in trials
- Decrease in functional status

# Use and effects of chemotherapy in elderly

## Analysis of SEER database 1997-2002



% pts receiving CT :  
20.4% in 1997  
27.8% in 2002



# Phase III trial of weekly paclitaxel combined with monthly carboplatin vs single-agent therapy in patients age 70 to 89

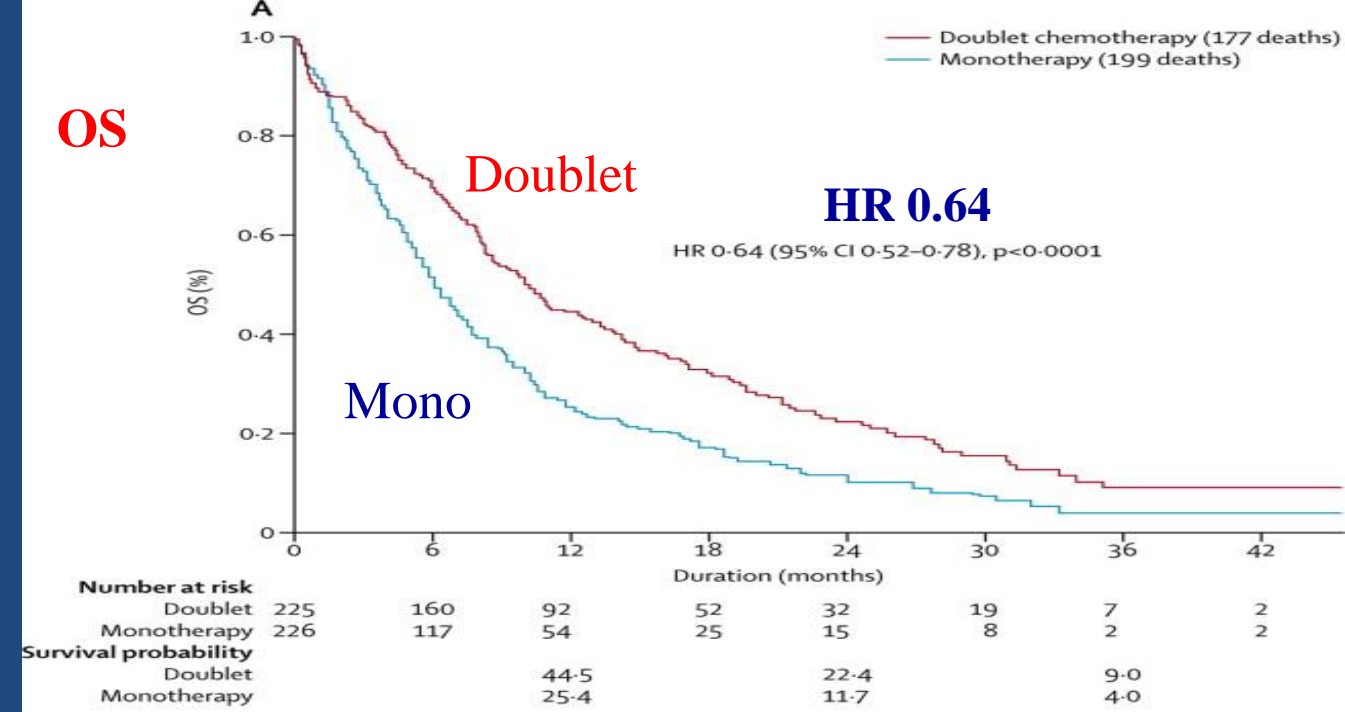


**PS 0-2**  
**N=451**  
**Median 77 yrs**



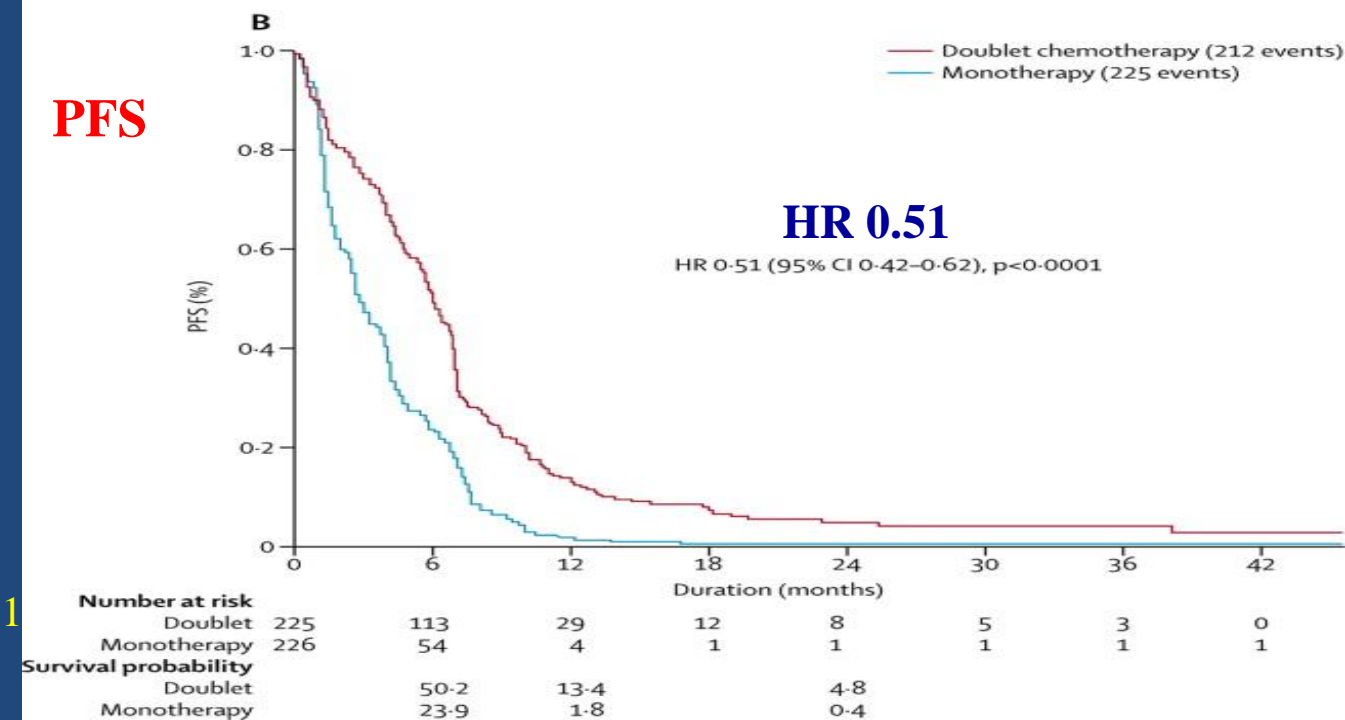
10.3 vs 6.2 months

OS

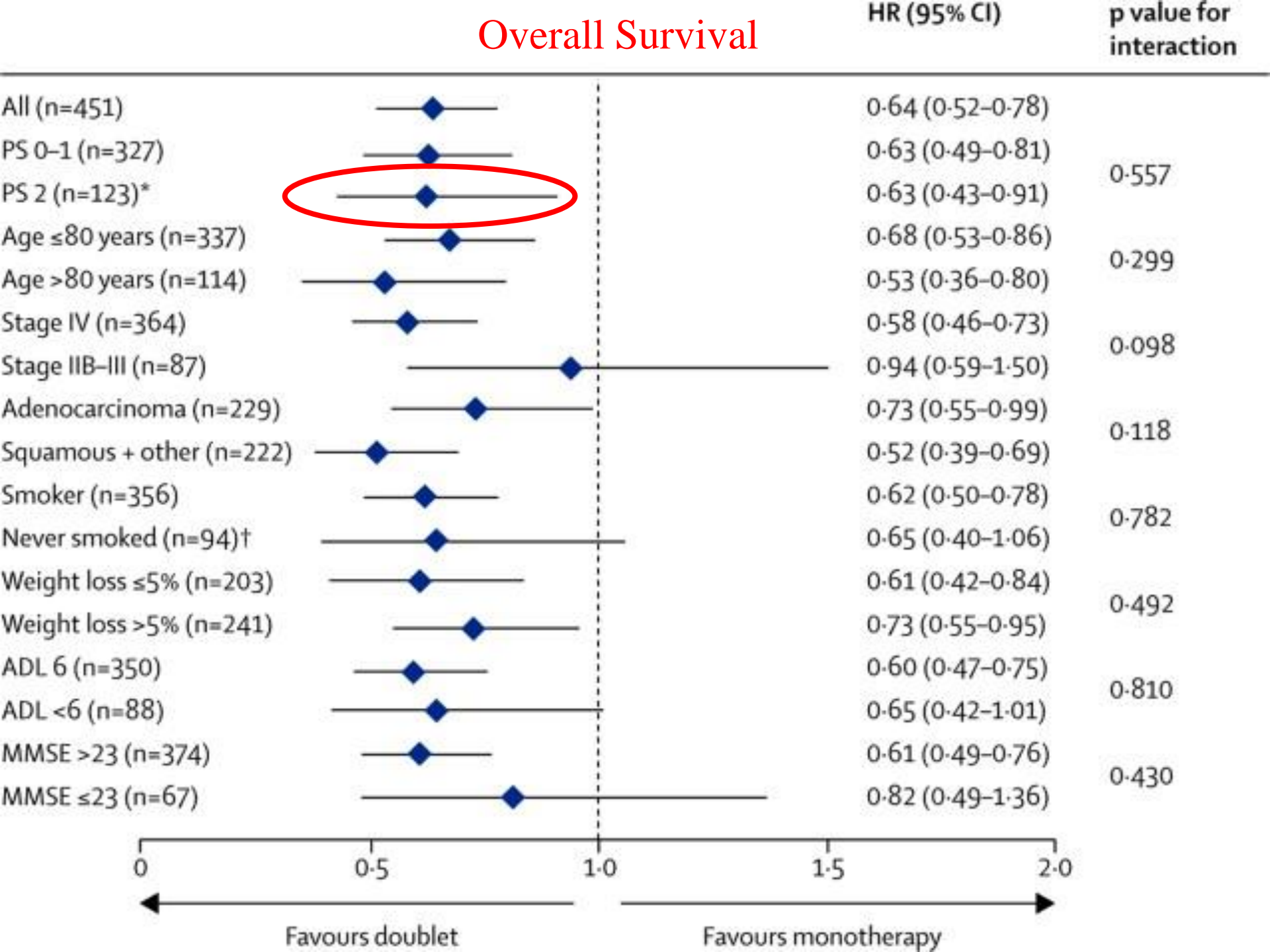


6.0 vs 2.8 months

PFS



# Overall Survival



# Conclusions

- PS 2 and elderly are specific and distinct populations
- Need for more reliable assessment tools
- Platinum based regimen represent SOC
  - Attenuated doses?
  - Weekly schedules?