Caring for the older patient with cancer

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Overview

- Cancer is the leading cause of death for those 60-79 years
- 60% of all cancers occur in patients who are 65 years or older
- Older individuals are more prone to develop cancer due to physiological changes associated with aging

Age 80 with High Risk Cancer: What treatment will you recommend?

To weigh the risks and benefits

→

Functional Age vs. Chronological Age

What is old?

65

Remaining Life Expectancy

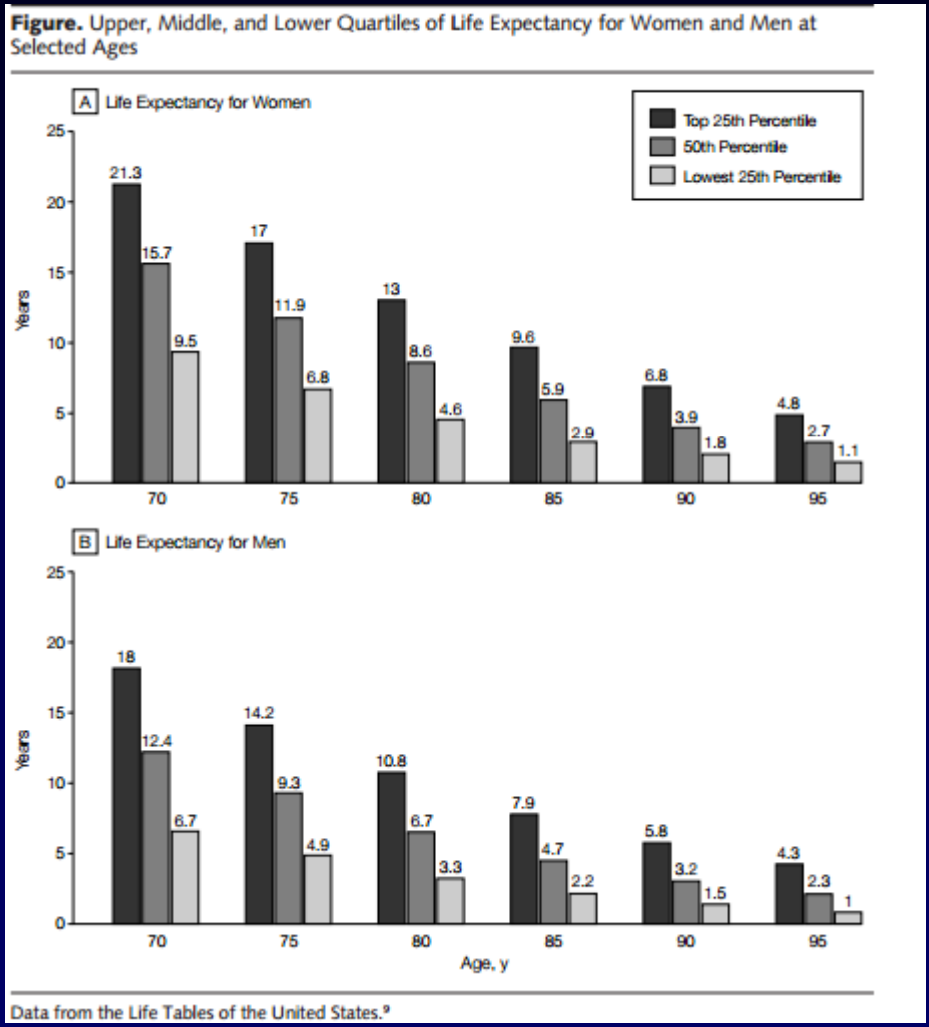


Figure. Upper, Middle, and Lower Quartiles of Life Expectancy for Women and Men at Selected Ages

Data from the Life Tables of the United States.[9]

Walter et al. JAMA 2001

Initial Assessment

- Who is the patient?
- What are the co-morbidities?
- What is the risk for chemotherapy toxicity?
- Are the risk factors modifiable?

→ **Perform a Geriatric Assessment**

Geriatric Assessment

Factors other than chronological age that predict morbidity & mortality in older adults

- Functional status
- Comorbid medical conditions
- Cognition
- Nutritional status
- Psychological state
- Social support
- Medications (polypharmacy)

→ **Comprehensive Geriatric Assessment (CGA)**

Geriatric Assessment: Functional Status
Activities of Daily Living (ADLs)

Basic self-care skills

Dressing

Bathing

Toileting

Transfer

Continence

Eating

Assistance with ADLs

Predictive of:

- Prolonged hospital stay
- Worsening of function in the hospital
- Greater home care use
- Nursing home placement
- Death

Functional dependence associated with ↓ survival:

Assistance in ≥ 1 ADLs: average life expectancy of < 3 yrs

Narain et al, JAGS 1988

Geriatric Assessment: Functional Status
Instrumental Activities of Daily Living

Higher order function

Required to maintain independence in the community

Shopping

Housekeeping

Transportation

Laundry

Telephone

Finances

Medications

Assistance in IADLs

- Understanding need for assistance with IADLs is critical for cancer treatment planning:
  - Transportation
  - Medications
- Predicts survival in older patients with NSCLC

Balducci et al, the Oncologist 2000

Maione et al, JCO 2005

Impact of functional status on survival

VOLUME 23 · NUMBER 28 · OCTOBER 1 2005

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Pretreatment Quality of Life and Functional Status Assessment Significantly Predict Survival of Elderly Patients With Advanced Non–Small-Cell Lung Cancer Receiving Chemotherapy: A Prognostic Analysis of the Multicenter Italian Lung Cancer in the Elderly Study

Paolo Maione, Francesco Perrone, Ciro Gallo, Luigi Manzione, FrancoVito Piantedosi, Santi Barbera, Silvio Cigolari, Francesco Rosetti, Elena Piazza, Sergio Federico Robbiati, Oscar Bertetto, Silvia Novello, Maria Rita Migliorino, Adolfo Favaretto, Mario Spatafora, Francesco Ferraù, Luciano Frontini, Alessandra Bearz, Lazzaro Repetto, and Cesare Gridelli

From the S Giuseppe Moscati Hospital, Avellino; National Cancer Institute;

Impact of functional status on survival

Table 3. Multivariate Analysis

Variable	HR	95% CL Upper	95% CL Lower	P*
Sex				.07
Male (n = 465)	Ref			
Female (n = 101)	0.78	0.59	1.02	
Age, years				.69
< 75 (n = 337)	Ref			
75-79 (n = 210)	1.09	0.89	1.32	
≥ 80 (n = 19)	0.96	0.57	1.64	
Performance status				.006
0-1 (n = 460)	Ref			
2 (n = 106)	1.46	1.12	1.88	
Charlson score				.66
0 (n = 237)	Ref			
1 (n = 210)	1.06	0.85	1.32	
2 (n = 92)	1.12	0.85	1.48	
≥ 3 (n = 27)	0.84	0.52	1.36	
ADL				.44
No dependence (n = 482)	Ref			
One or more dependence (n = 84)	1.13	0.85	1.47	
IADL				.04
Better (n = 188)	Ref			
Intermediate (n = 217)	0.97	0.76	1.22	
Worse (n = 161)	1.31	1.00	1.71	
Quality of Life				.0003
Better (n = 119)	Ref			
Intermediate (n = 294)	1.62	1.24	2.10	
Worse (n = 153)	1.76	1.29	2.39	
Stage				.71
IIIb (n = 178)	Ref			
IV (n = 388)	1.04	0.85	1.28	
Histotype				.17
Other (n = 314)	Ref			
Squamous (n = 252)	1.14	0.94	1.39	
No. of sites of disease				.02
For each added site	1.13	1.02	1.24	
Center by No. of enrolled patients				.09
< 10 (n = 148)	Ref			
10-29 (n = 259)	1.19	0.94	1.52	
≥ 30 (n = 159)	1.34	1.03	1.74	

Better values of baseline QoL (P.0003) and IADL (P.04) were significantly associated with better prognosis, whereas ADL (P.44) and Charlson score (P.66) had no prognostic value. Performance status 2 (P.006) and a higher number of metastatic sites (P.02) also predicted shorter overall survival.

Assistance with IADLs → Worse Survival in Patients with Lung Cancer

Categories of IADLs:

- Better:

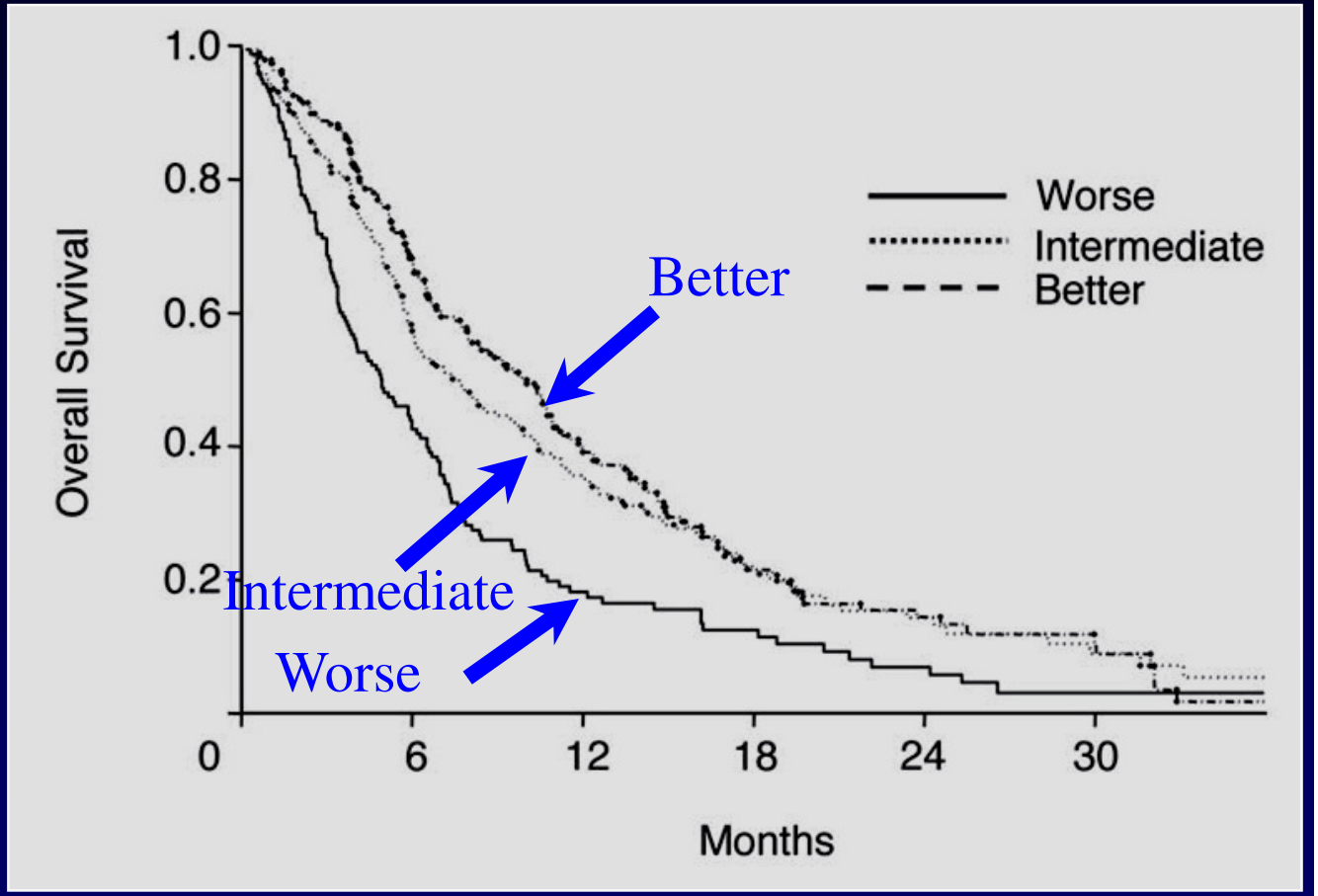
  Score of 100%

- Intermediate:

  Score of 51-99%

- Worse:

  Score of 0-50%



Maione et al, J Clin Oncol, 2005

Predicting the Risk of Chemotherapy Toxicity in Older Patients: The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score

Table 2. Selection of Individual Variables Associated With Hematologic or Nonhematologic Toxicity[a]

	Hematologic Toxicity		Nonhematologic Toxicity	
Biomarker	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	0.99 (0.94-1.05)	.83	1.01 (0.96-1.06)	.76
Sex	0.68 (0.37-1.30)	.25	1.28 (0.83-1.98)	.27
BMI	0.03 (0.97-1.08)	.33	0.99 (0.95-1.04)	.84
Diastolic BP	1.30 (1.02-1.65)	.03[b]	1.00 (0.98-1.02)	.96
CIRS Severity Index	1.08 (0.61-1.91)	.78	1.09 (0.66-1.81)	.73
Polypharmacy	1.00 (0.94-1.07)	.93	1.03 (.97-1.08)	.35
WBC	1.02 (0.98-1.06)	.33	0.98 (0.94-1.03)	.45
Hemoglobin	0.99 (0.85-1.15)	.91	0.90 (0.79-1.03)	.12[b]
Lymphocytes	1.05 (0.98-1.12)	.20[b]	0.95 (0.85-1.05)	.32
AST	1.01 (1.00-1.01)	.14[b]	1.00 (1.00-1.01)	.43
CrCL	1.0 (0.99-1.01)	.74	0.84 (0.69-1.03)	.09
Albumin	0.76 (0.44-1.30)	.39	0.74 (0.45-1.20)	.22[b]
LDH	1.41 (1.17-1.86)	.004[b]	1.00 (1.00-1.00)	.69
Self-rated health	1.02 (0.80-1.29)	.89	0.87 (0.71-1.07)	.19[b]
ECOG PS	1.13 (0.81-1.57)	.47	1.41 (1.05-1.89)	.03[b]
IADL	0.77 (0.58-1.03)	.08[b]	0.98 (0.91-1.06)	.58
MNA	0.99 (0.92-1.06)	.69	0.73 (0.60-.90)	.003[b]
MMS	0.97 (0.87-1.07)	.51	0.77 (0.63-93)	.008[b]
GDS	1.00 (0.91-1.12)	.94	1.04 (0.95-1.14)	.44
Tumor stage	1.00 (0.77-1.30)	.99	1.10 (0.87-1.39)	.65
Bone marrow invasion	1.19 (0.61-2.33)	.62	1.46 (0.78-2.72)	.26
Prior chemotherapy	1.30 (0.75-2.24)	.35	0.85 (0.53-1.36)	.50
Tumor response	0.96 (0.66-1.4)	.83	1.16 (0.84-1.63)	.44
Chemotox	2.20 (1.72-2.81)	<.001[b]	1.13 (0.93-1.37)	.23[b]

Table 4. The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score

	Points		
Predictors	0	1	2
Hematologic score[a]			
Diastolic BP	≤72	>72	
IADL	26-29	10-25	
LDH (if ULN 618 U/L; otherwise, 0.74 /L*ULN)	0-459		>459
Chemotox[b]	0-0.44	0.45- 0.57	>0.57
Nonhematologic score[a]			
ECOG PS	0	1-2	3-4
MMS	30		<30
MNA	28-30		<28
Chemotox[b]	0-0.44	0.45-0.57	>0.57

Extermann et al. Cancer. 2012

Predictors of chemotherapy toxicity

Geriatric Assessment Variables

1. Falls in the last six months
2. Limitations in walking one block
3. Need for assistance with taking medications
4. Decreased social activities

Hurria et al, J Clin Oncol, 2011

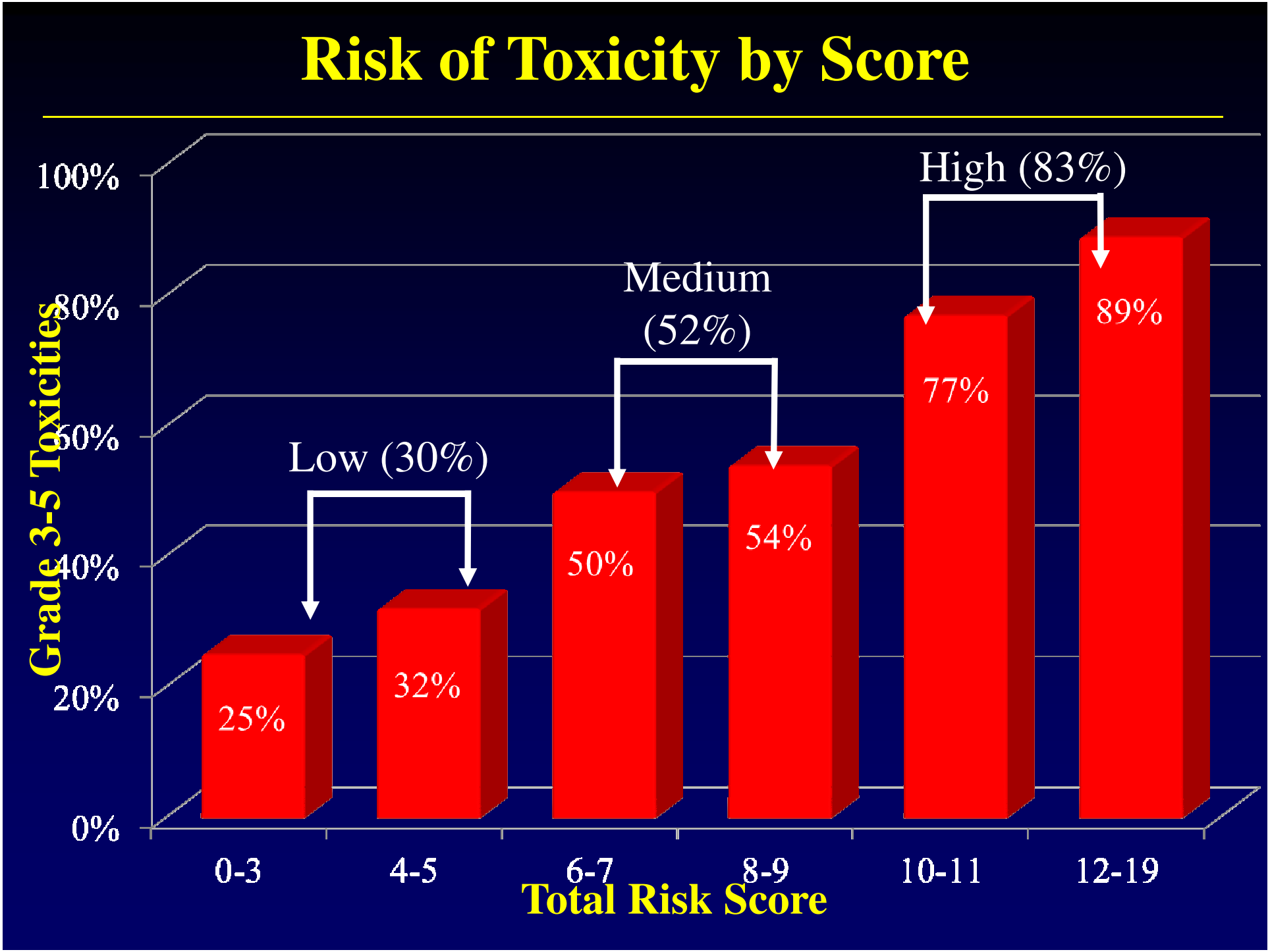
CARG model for predicting chemotherapy toxicity in older adults

Risk factor	Prevalence		Grades 3 to 5 toxicity		OR	95% CI	Score
	No.	Percent	No.	Percent			
Age ≥72 years	270	54	163	60	1.85	1.22 to 2.82	2
Cancer type GI or GU	185	37	120	65	2.13	1.39 to 3.24	2
Chemotherapy dosing, standard dose	380	76	204	54	2.13	1.29 to 3.52	2
Number of chemotherapy drugs, polychemotherapy	351	70	192	55	1.69	1.08 to 2.65	2
Hemoglobin <11 g/dL (male), <10 g/dL (female)	62	12	46	74	2.31	1.15 to 4.64	3
Creatinine clearance (Jelliffe, ideal weight) <34 mL/min	44	9	34	77	2.46	1.11 to 5.44	3
Hearing, fair or worse	123	25	76	62	1.67	1.04 to 2.69	2
Number of falls in last six months, one or more	91	18	61	67	2.47	1.43 to 4.27	3
IADL: Taking medications, with some help/unable	39	8	28	72	1.50	0.66 to 3.38	1
MOS: Walking one block, somewhat limited/limited a lot	109	22	69	63	1.71	1.02 to 2.86	2
MOS: Decreased social activity because of physical/emotional health, limited at least sometimes	218	44	126	58	1.36	0.90 to 2.06	1

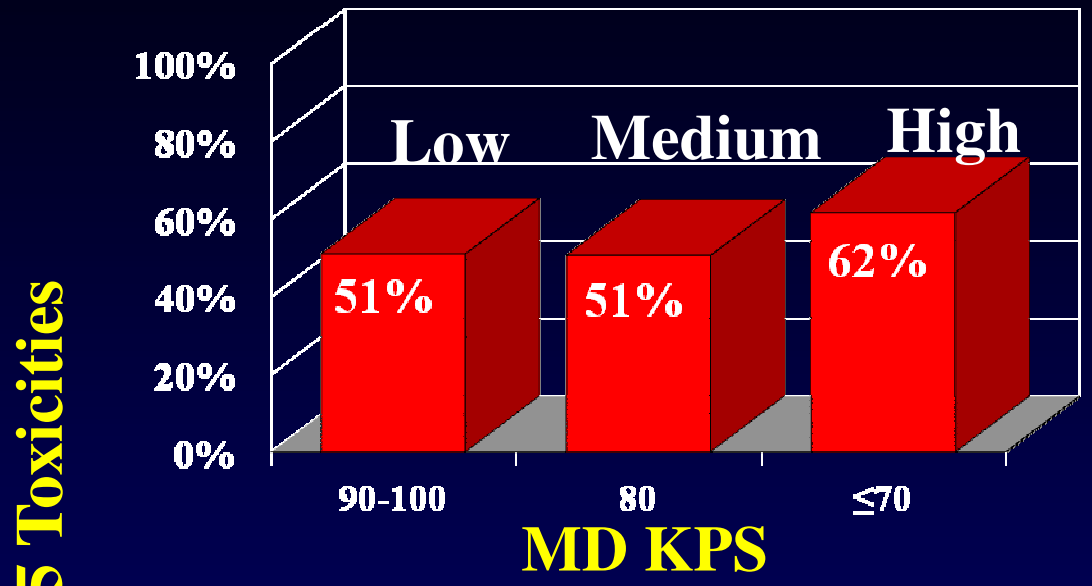
CARG: Cancer and Aging Research Group; OR: odds ratio; GI: gastrointestinal; GU: genitourinary; IADL: instrumental activities of daily living; MOS: Medical Outcomes Study.

From: Hurria A, Togawa K, Mohile SG, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. J Clin Oncol 2011; 29:3457. Reprinted with permission.

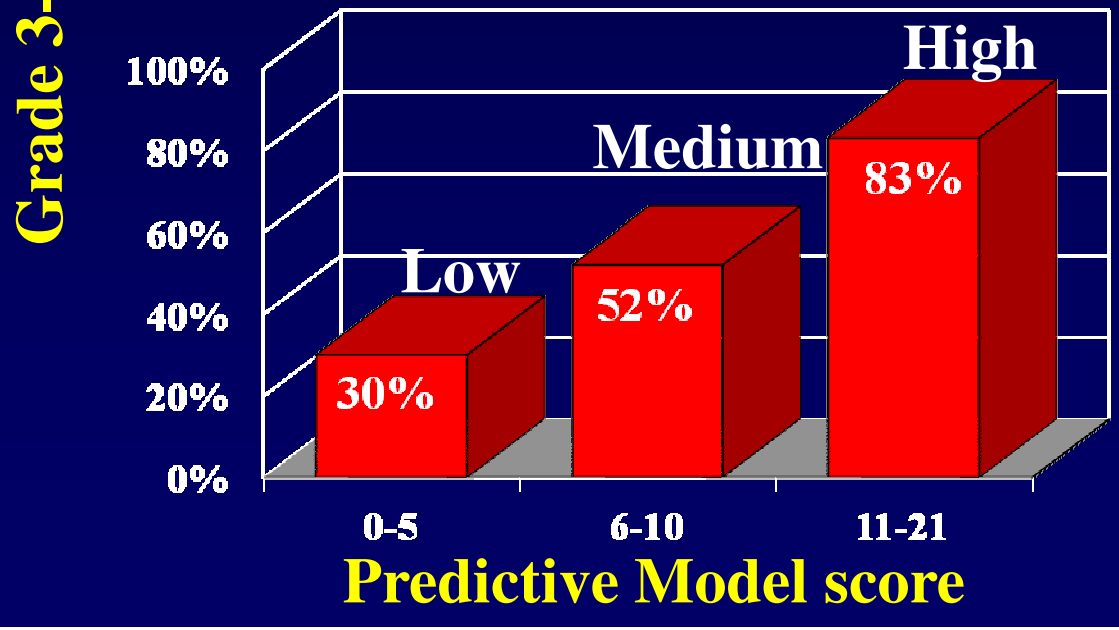
Risk of Toxicity by Score



MD-rated KPS vs. Predictive Model



Chi-square test $p=0.19$



Chi-square test $p<.0001$

Updated Recommendations of SIOG on Breast Cancer in elderly patients: 2010

- General health and functional status can be captured in a multidomain geriatric assessment
- A screening assessment is a reasonable first step in identifying patients that may benefit from an extended CGA
- Active intervention for CGA-identified reversible geriatric domains can reduce morbidity and mortality, and improve quality of life
- Serial geriatric assessment can identify incident deterioration, for which intervention might improve outcomes

The G8 Screening Questionnaire

	Items	Possible answers (score)
A	Has food intake declined over the past 3 months due to loss of appetite, digestive problems or chewing or swallowing difficulties?	0: severe decrease in food intake 1: moderate decrease in food intake 2: no decrease in food intake
B	Weight loss during the last 3 months	1: weight loss>3 kg 1: does not know 2: weight loss between 1 and 3 kg 3: no weight loss
C	Mobility	0: bed or chair bound 1: able to get out of bed/chair but does not go out 2: goes out
E	Neuropsychological problems	0: severe dementia or depression 1: mild dementia or depression 2: no psychological problems
F	Body Mass Index	0: BMI <18.5 1: BMI 18.5-<21 2: BMI 21 to <23 3: BMI 23 and >23
H	Takes more than 3 prescription drugs per day	0: yes 1: no
P	In comparison with other people of the same age, how do they consider their health status?	0: not as good 0.5: does not know 1: as good 2: better
	Age	0: >85 yr 1: 80-85 yr 2: <85 yr
Total Score		0-17

- 8 questions
- Nurse administered
- Takes 5-10 min to perform
  - -Appetite, weight loss, BMI
  - -Mobility
  - -Mood and cognition
  - -Number of medications
  - -Patient-related health
  - -Age categories
- Abnormal if score <14
  - -Preliminary analysis
  - -Sensitivity: 89.6%
  - -Specificity: 60.4%

Bellera et al, Ann Oncol, 2012

Flemish TRST Screening Tool

Item	Score	
	Yes	No
Presence of cognitive impairment (disorientation, diagnosis of dementia, or delirium)	2	0
Lives alone or no caregiver available, willing or able	1	0
Difficulty with walking or transfers or falls in the past 6 months	1	0
Hospitalized in the last 3 months	1	0
Polypharmacy: > 5 medications	1	0

Score >2 indicates a high risk geriatric profile

Kenis et al, Crit Rev Oncol Hematol, 2006

The Vulnerable Elders Survey (VES) 13 scale

Domain	Score
Age	
75-85	1
>85	3
Self-rated health	
Good, very good, and excellent	0
Fair and poor	1
ADL/IADL	
Needs assistance with	
Bathing or showering	1
Shopping	1
Money management	1
Transfer	1
Light housework	1
Difficulty in special activities	
Kneeling, bending and stooping	1
Performance of housework	1
Reaching out and lifting upper extremities above the shoulder	1
Lifting and carrying 10 pounds	1
Walking ¼ of a mile	1
Writing or handling and grasping small objects	1

Score >3: Vulnerable Elderly

Saliba et al, J Am Geriatr Soc 2001

Geriatric Assessment: Comorbidity

Definition:

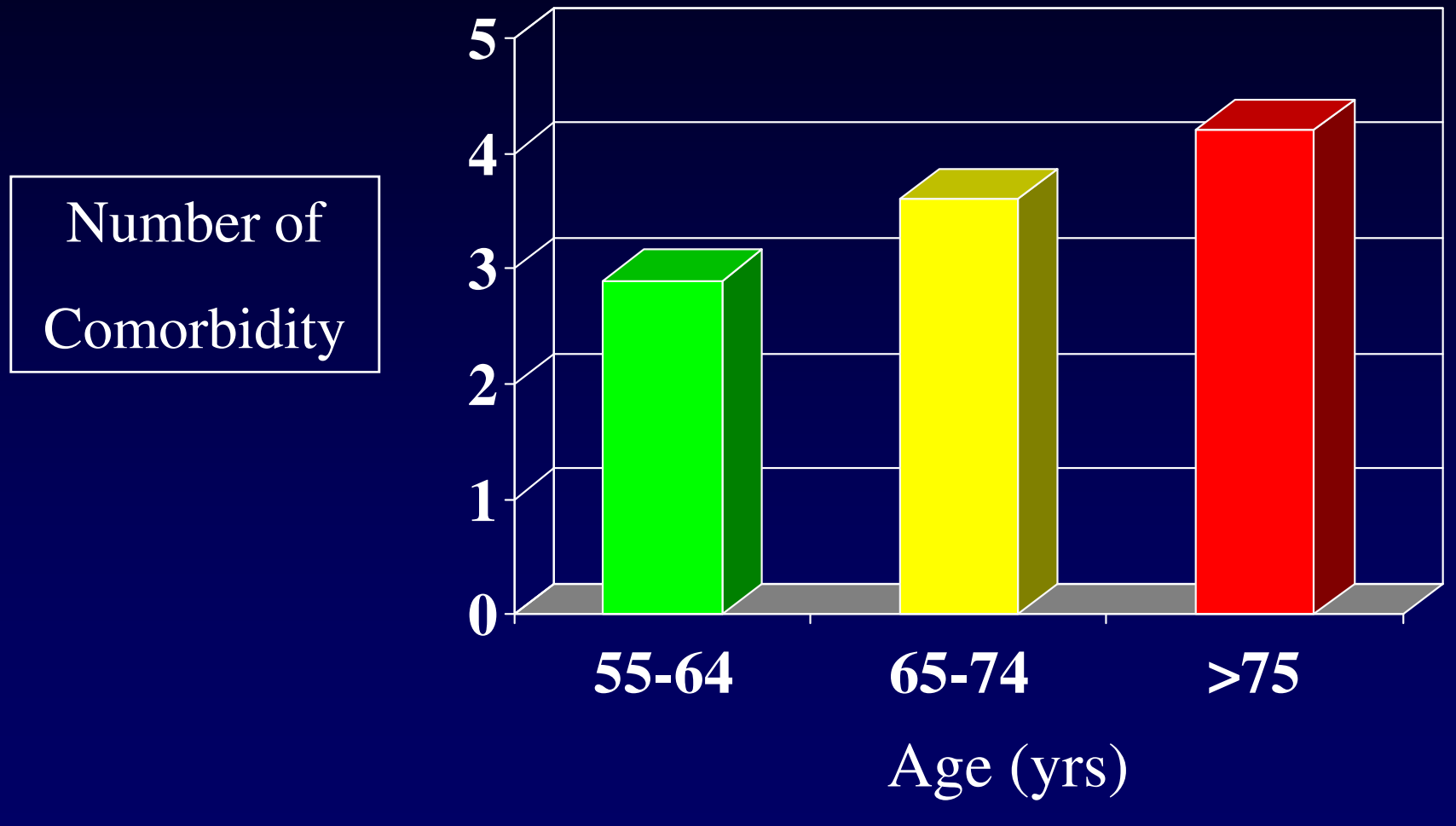
Concurrent, independent health condition which may be a predictor of survival and resource requirements

Questions:

1) Is the patient going to die from cancer or another medical problem?

2) Will another medical problem limit the ability to tolerate chemotherapy?

Comorbidity Increases with Age



Yancik et al, Cancer 1997

Charlson Comorbidity Index

Charlson risk index

Condition	Assigned weights for diseases
Myocardial infarct	1
Heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Connective tissue disease	1
Ulcer disease	1
Mild liver disease	1
Diabetes	1
Hemiplegia	2
Moderate or severe renal disease	2
Diabetes with end organ damage	2
Any tumor	2
Leukemia	2
Lymphoma	2
Moderate or severe liver disease	3
Metastatic solid tumor	6
AIDS	6
Weighted comorbidity classes	
Low	0 points
Medium	1 to 2 points
High	3 to 4 points
Very high	≥5 points

Adapted from: Charlson ME, Pompei P, Ales KL, et al. J Chron Dis 1987; 40:373.

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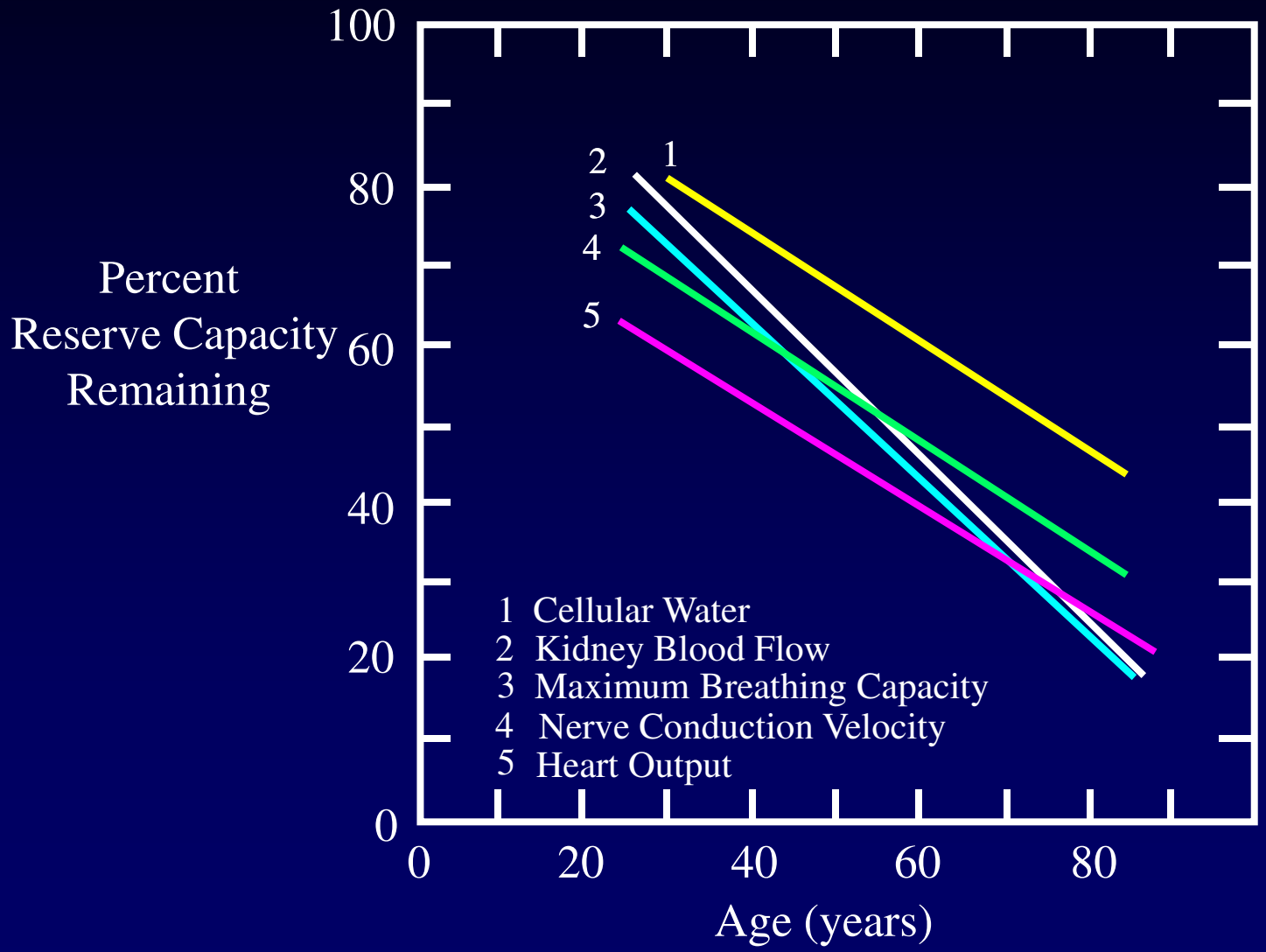
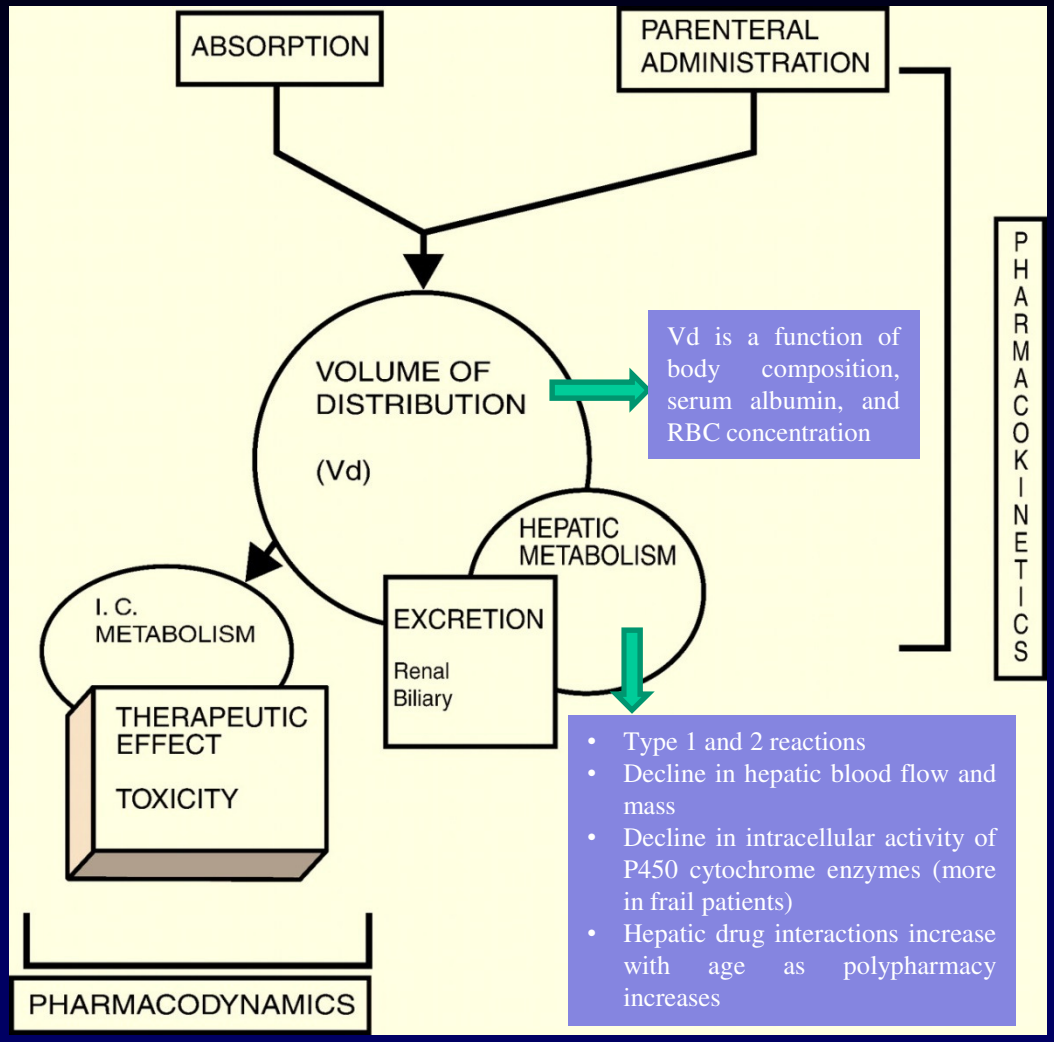
Charlson et al J Chron Dis 1987

Linear Decline Of Organ Reserve With Increasing Age



Baker and Martin, Geriatric Medicine, 1996

Drug Pharmacokinetics



Balducci L , and Extermann M, The Oncologist, 2000

The Oncologist

Calculating Creatinine Clearance

Creatinine Clearance Equations	
Cockroft & Gault Jeliffe	Commonly used Not validated in older adults
MDRD	More accurate in pts with chronic renal disease Ethnicity, BUN, & albumin are taken into account

None are perfect
All are better than creatinine alone

Hurria & Lichtman, BJC 2008

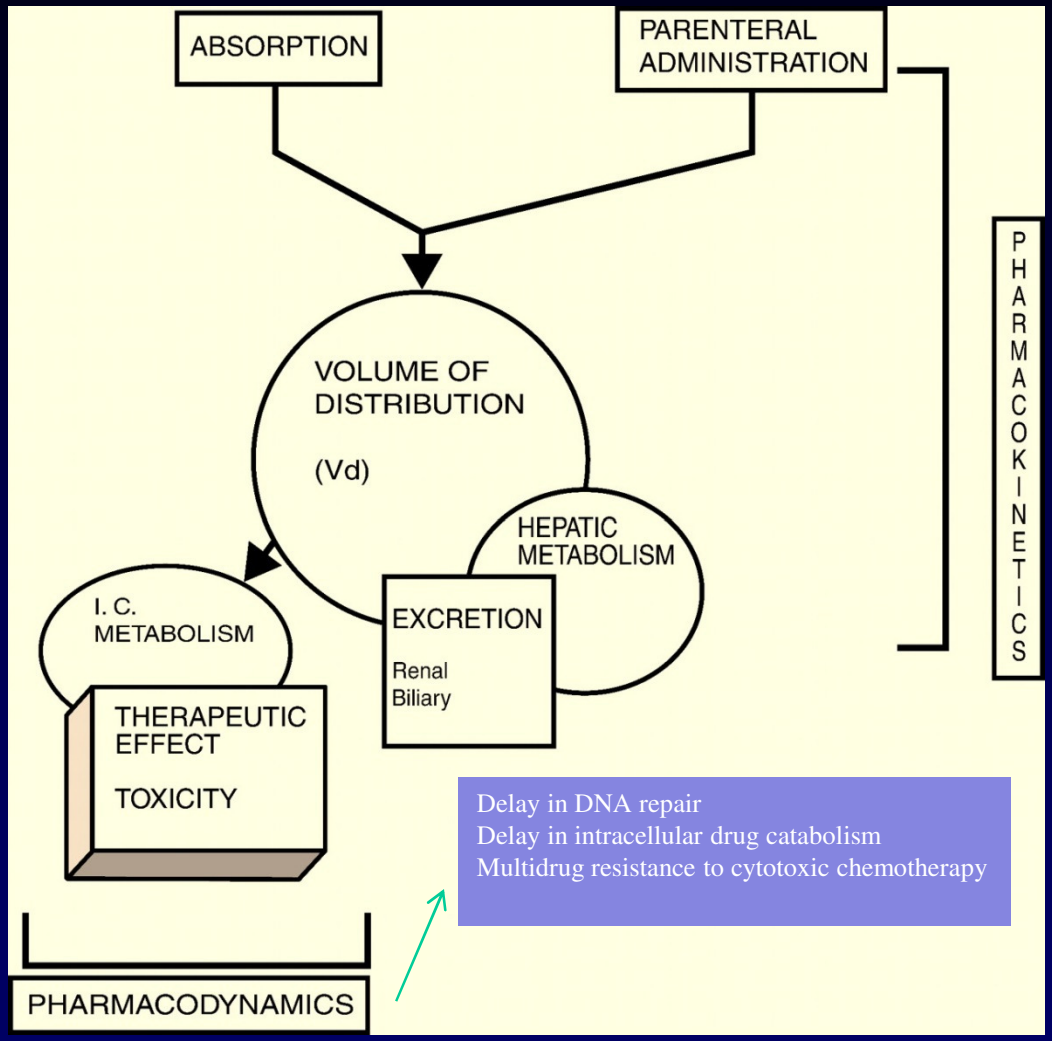
Renal Function Decreases with Aging

Example: Weight - 130 lbs

Age	Creatinine (mg/dL)	CrCl* (ml/min)
40	1.3	54
50	1.3	48
60	1.3	43
70	1.3	38
80	1.3	31
90	1.3	27
100	1.3	21

Creatinine: Not an adequate measure of renal function

Drug Pharmacodynamics



Balducci L , and Extermann M, The Oncologist, 2000

The Oncologist

Provisions that may reduce complications of cytotoxic chemotherapy in older cancer patients

A. Antidotes	
Antidote	Indication
G-CSF; GM-CSF	Patients aged 70 and older receiving moderately toxic chemotherapy (CHOP, CA)
Erythropoietin	Patients aged 70 and older to maintain hemoglobin levels ≥12 gm/dl
IL-11	Patients with solid tumors who have needed platelet transfusions
Amifostine	To prevent nephrotoxicity from high doses of cisplatin
	To prevent salivary toxicity in patients with head and neck cancer receiving radiation therapy
Desrazoxane	Patients for whom a dose of doxorubicin ≥300 mg/m^2 is expected

B. PK changes	
PK intervention	Indication
Dose adjustment to GFR	Drugs for which the parent compound or an active metabolite is excreted through the kidneys when:
	• The patient has experienced a grade IV toxicity during the previous administration of the drug
	• The patient is considered at high risk for complications according to the geriatric evaluation
	• The patient presents an abnormal serum creatinine
Continuous infusion or low daily doses of anthracyclines	No specific indications
Low weekly doses of taxanes	As an alternative to full doses every three weeks in breast cancer

Balducci L , and Extermann M, The Oncologist, 2000

The Oncologist

Frailty: definition (Fried)

Operationally defined as:

A clinical syndrome in which **three or more** of the following are present:

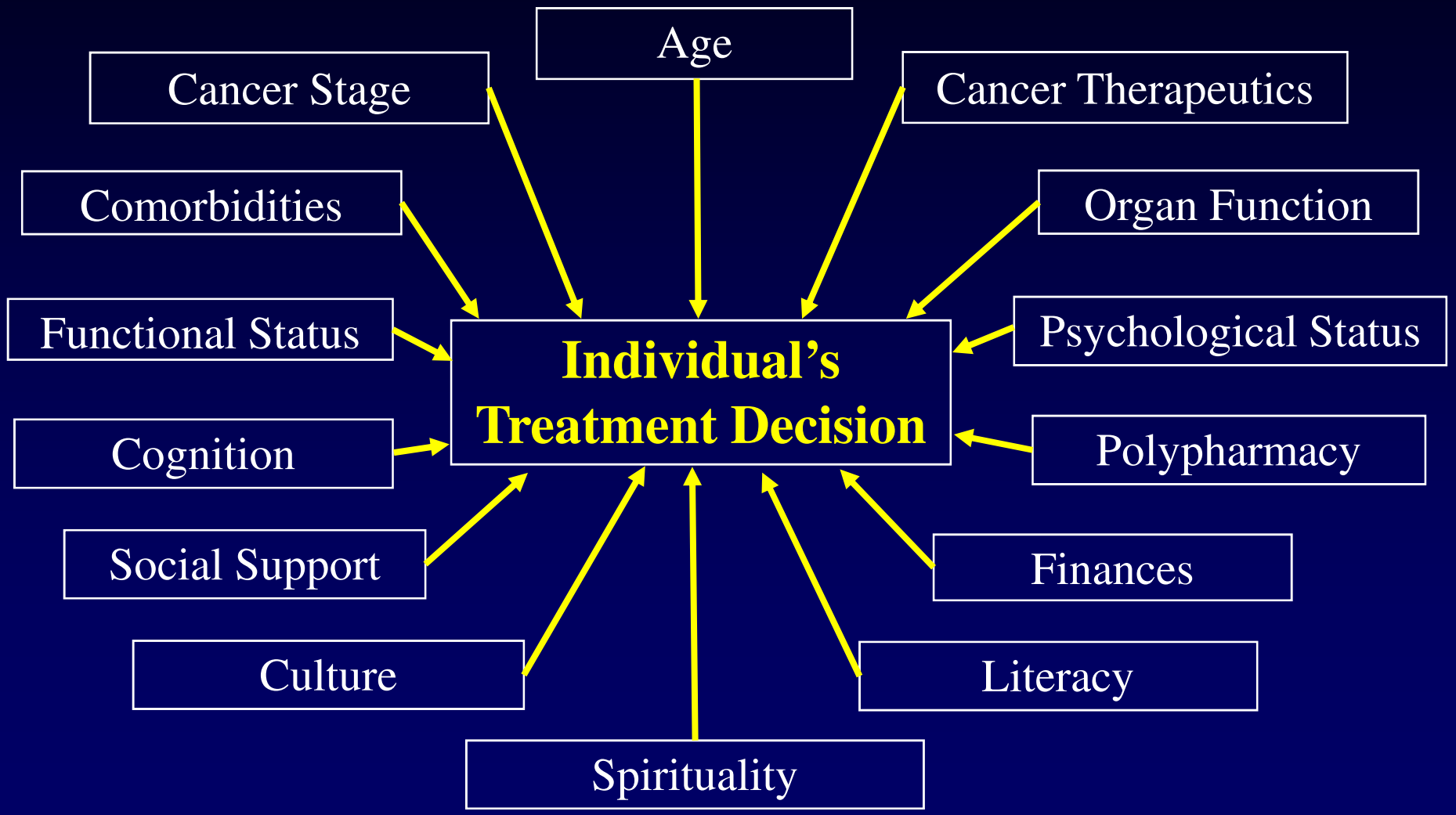
- unintentional weight loss (10lbs/4.5kgs in last year)
- self-reported exhaustion
- weakness (grip strength)
- slow walking speed
- low physical activity

Fried et al. Frailty in older adults: evidence for a phenotype. J Geront 2001;56:M146-M156

Why is measurement of frailty important?

- Frailty predicts:
  - falls
  - ED visits and hospitalisation
  - entry into residential care
  - death
- Frailty stratification can predict risk of institutional care, or help plan interventions

Key Factors Contributing to Decision Making

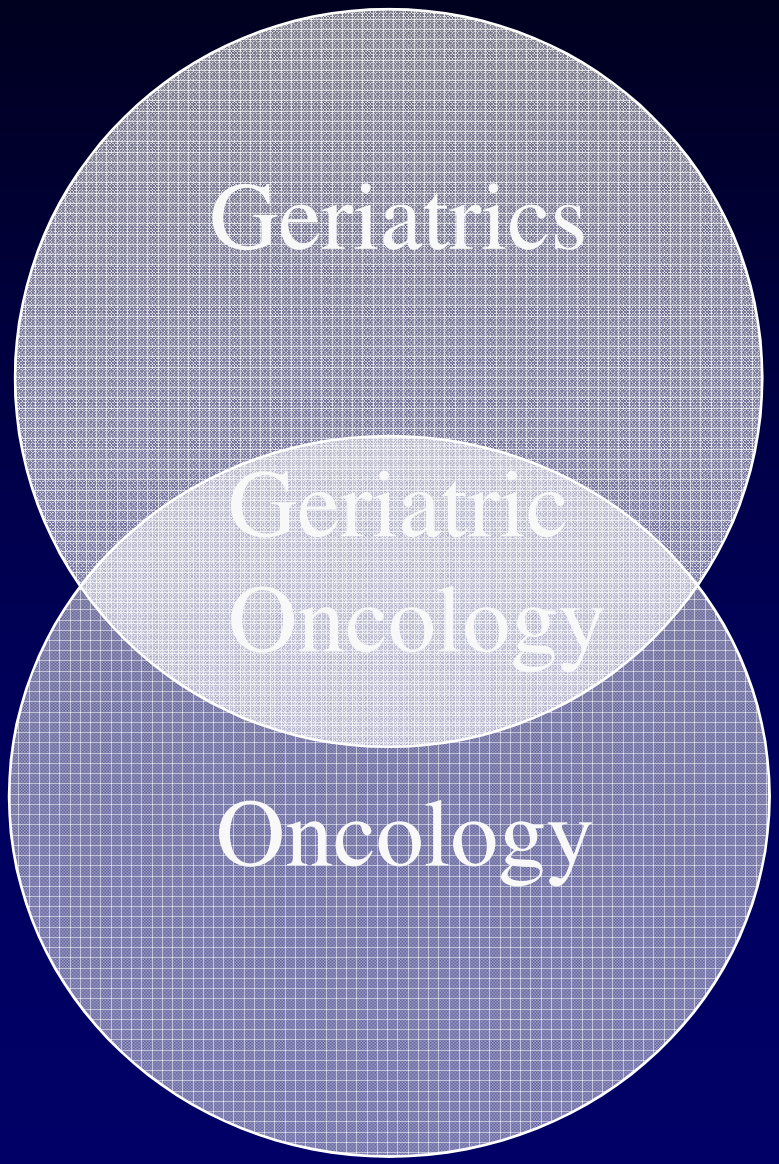


Conclusions

- Assessing an older adult for cancer therapy
  - Understanding the benefit
  - Quantifying the risks
  - Assessing capacity to make a decision
  - A geriatric assessment can help to obtain key information

- Decision to take therapy is an individual decision
  - Supporting the patient through the decision process

Thank you!




Questions ?