Assessing Older Adults with Cancer: Understanding Functional vs. Chronological Age

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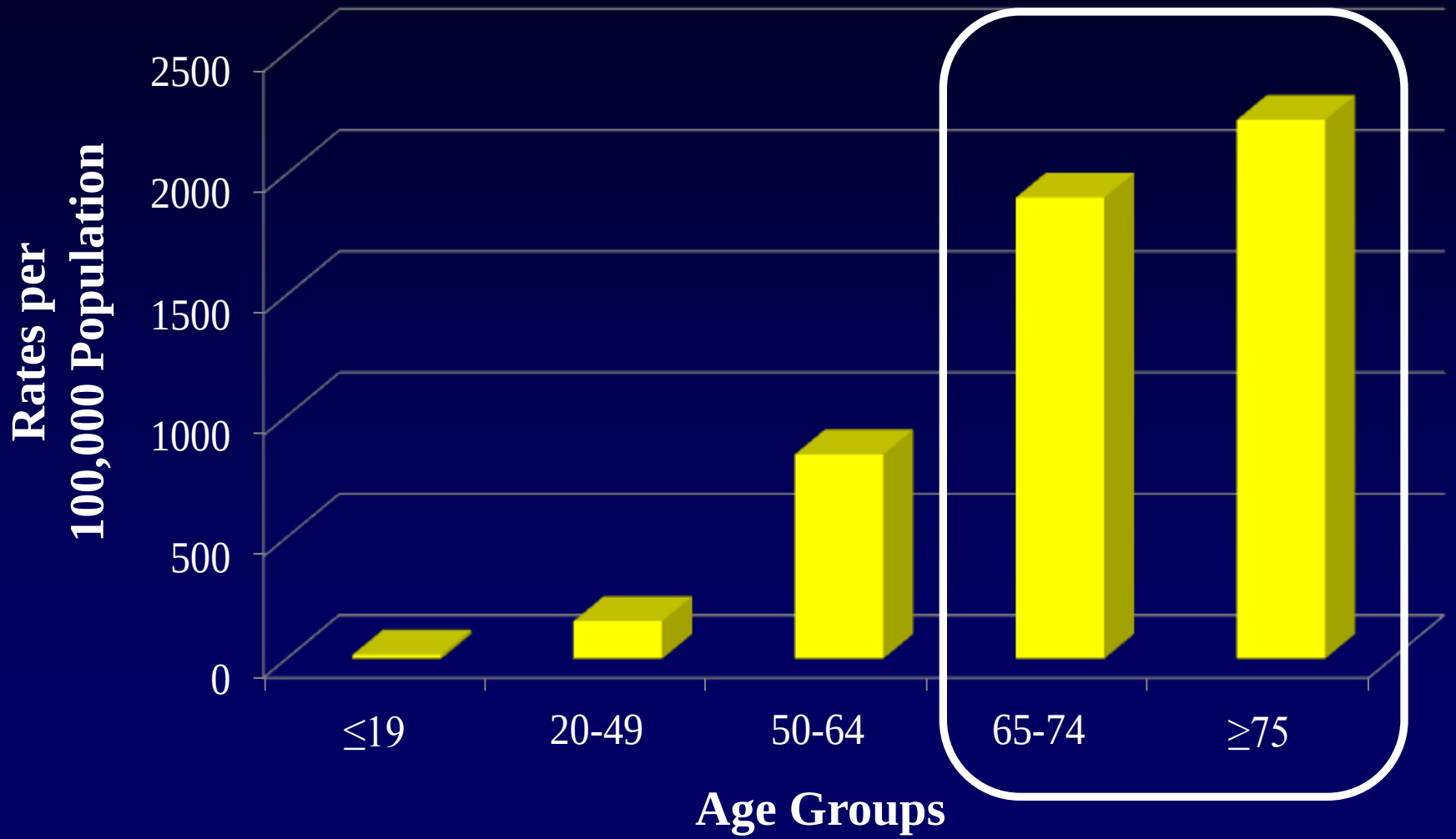
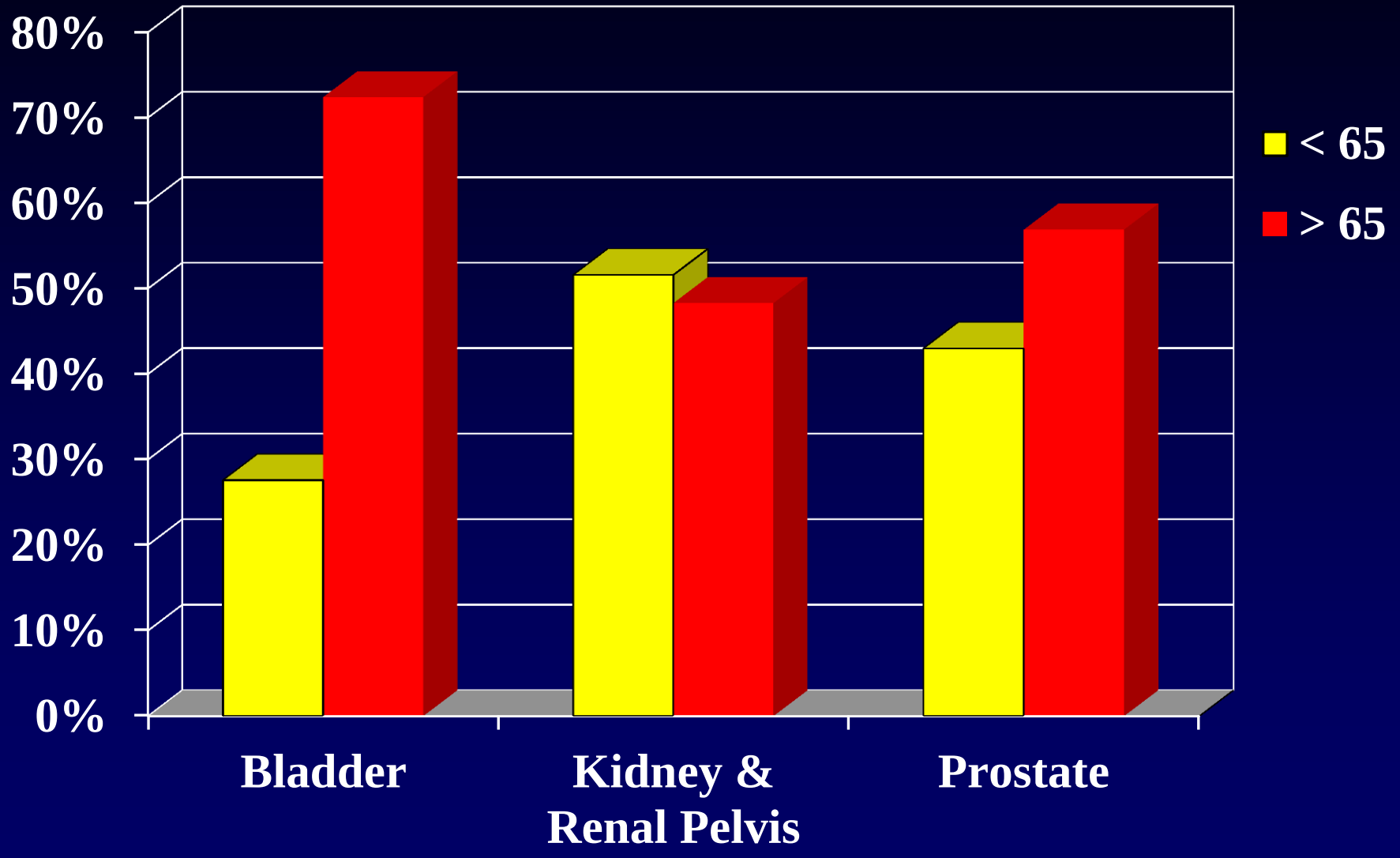
Cancer is a Disease Associated with Aging

60% of cancer occurs in people ≥ age 65



CDC, Morbidity and Mortality Weekly Report 2013

GU Cancer and Aging

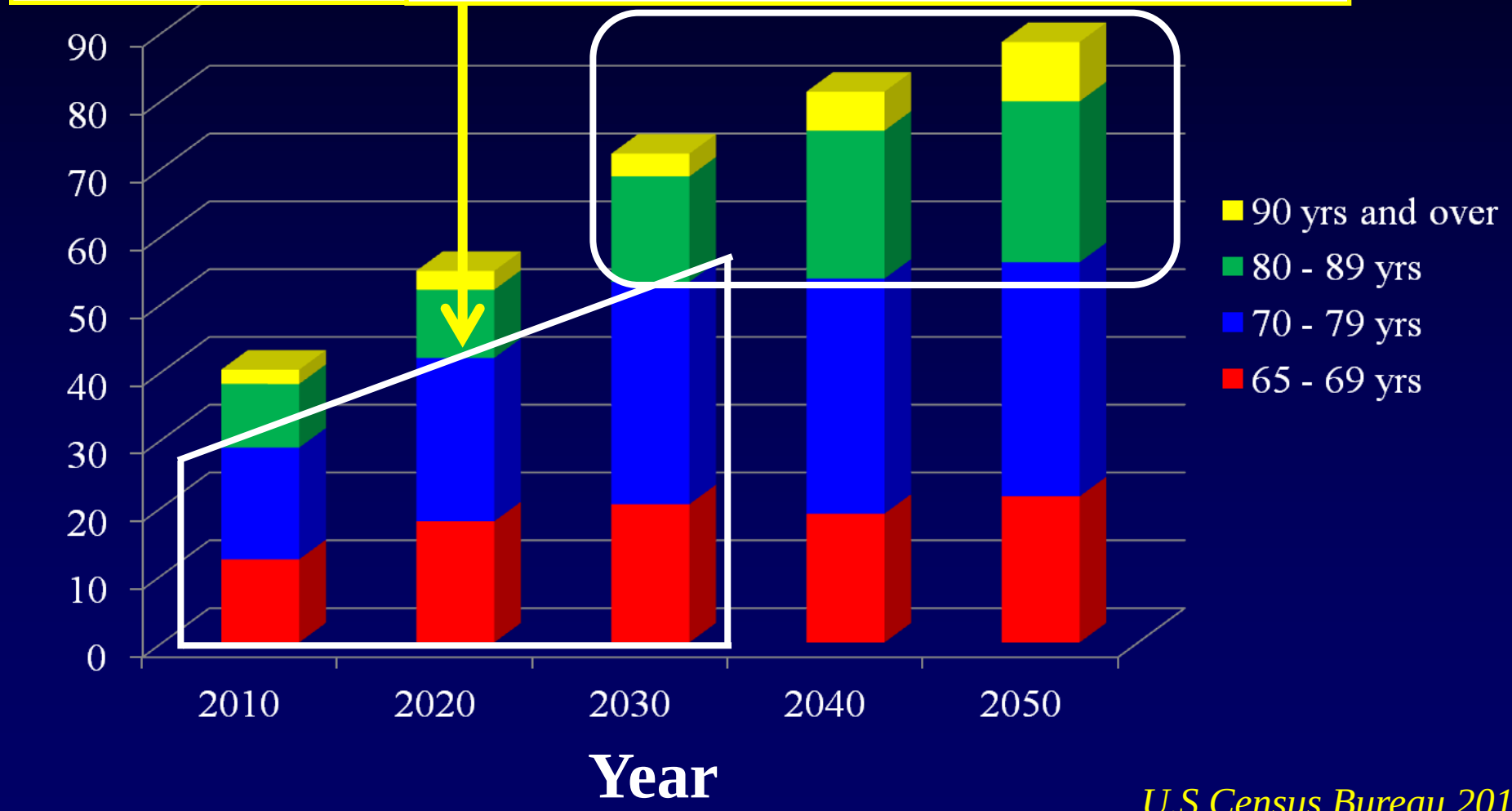


SEER 18 2007-2011

US Population Age ≥ 65 (millions)

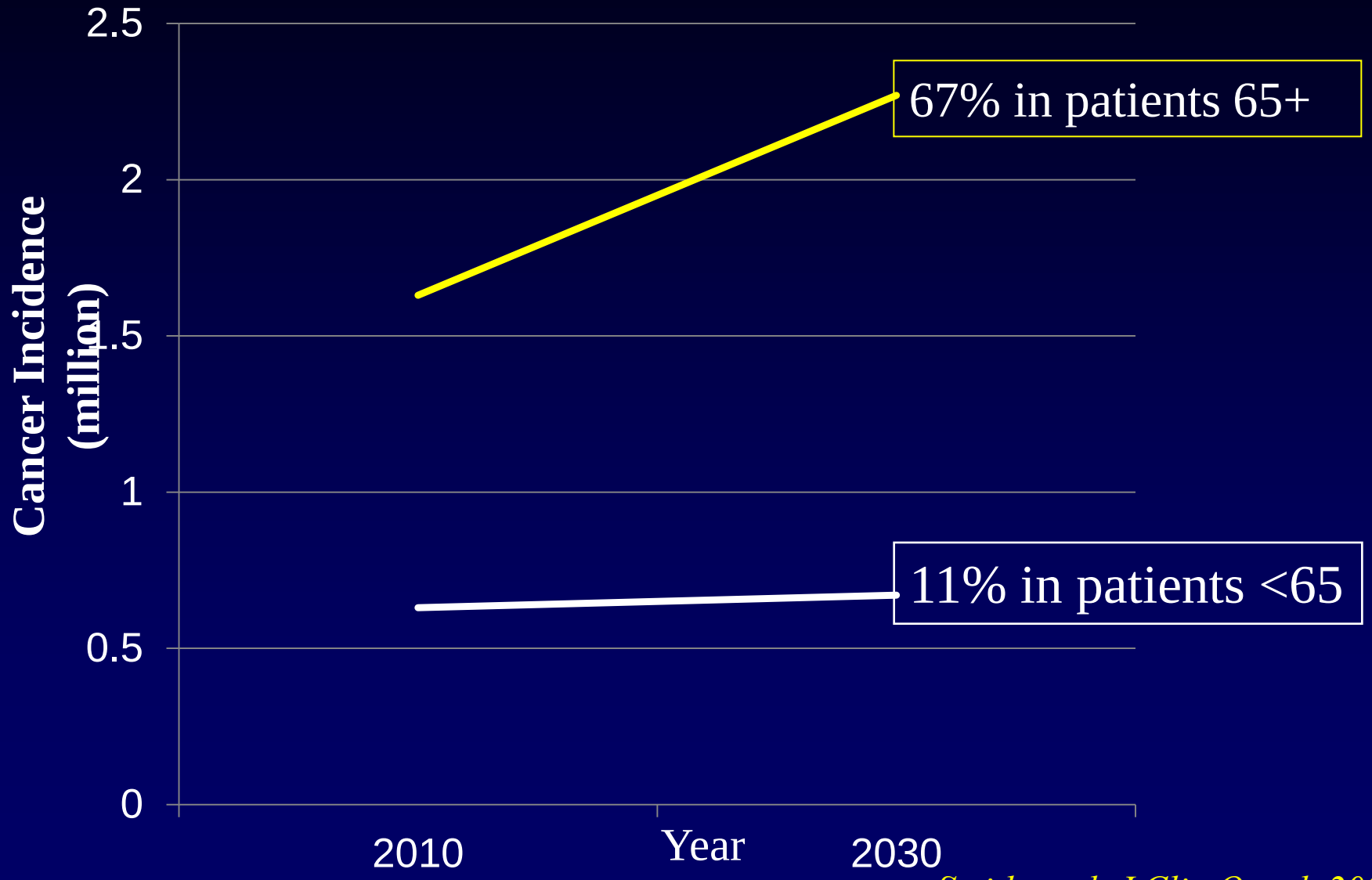
201
Largest growth in

Shift in 2030:
Largest growth in the 80+ age groups



U.S Census Bureau 2010

Projected Rise in Cancer Incidence from 2010 to 2030



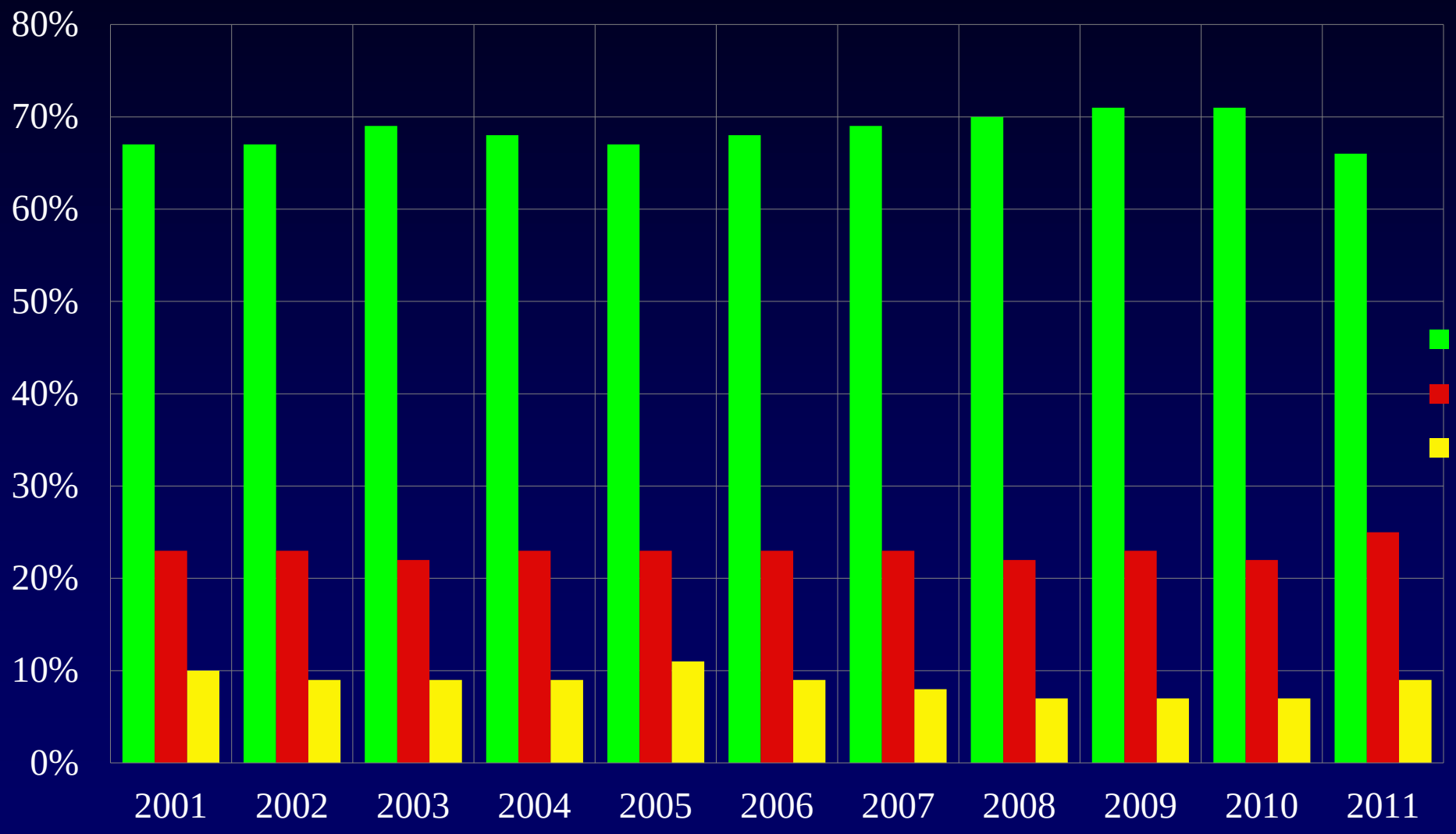
Smith et al, J Clin Oncol, 2009

The Population is Aging

The Number of Older Adults With Cancer is on the Rise

Are we prepared?

Few Patients Older Adults on NCI Trials
No Change Over Time



NCI/DCTD Clinical Data Update System, 2012

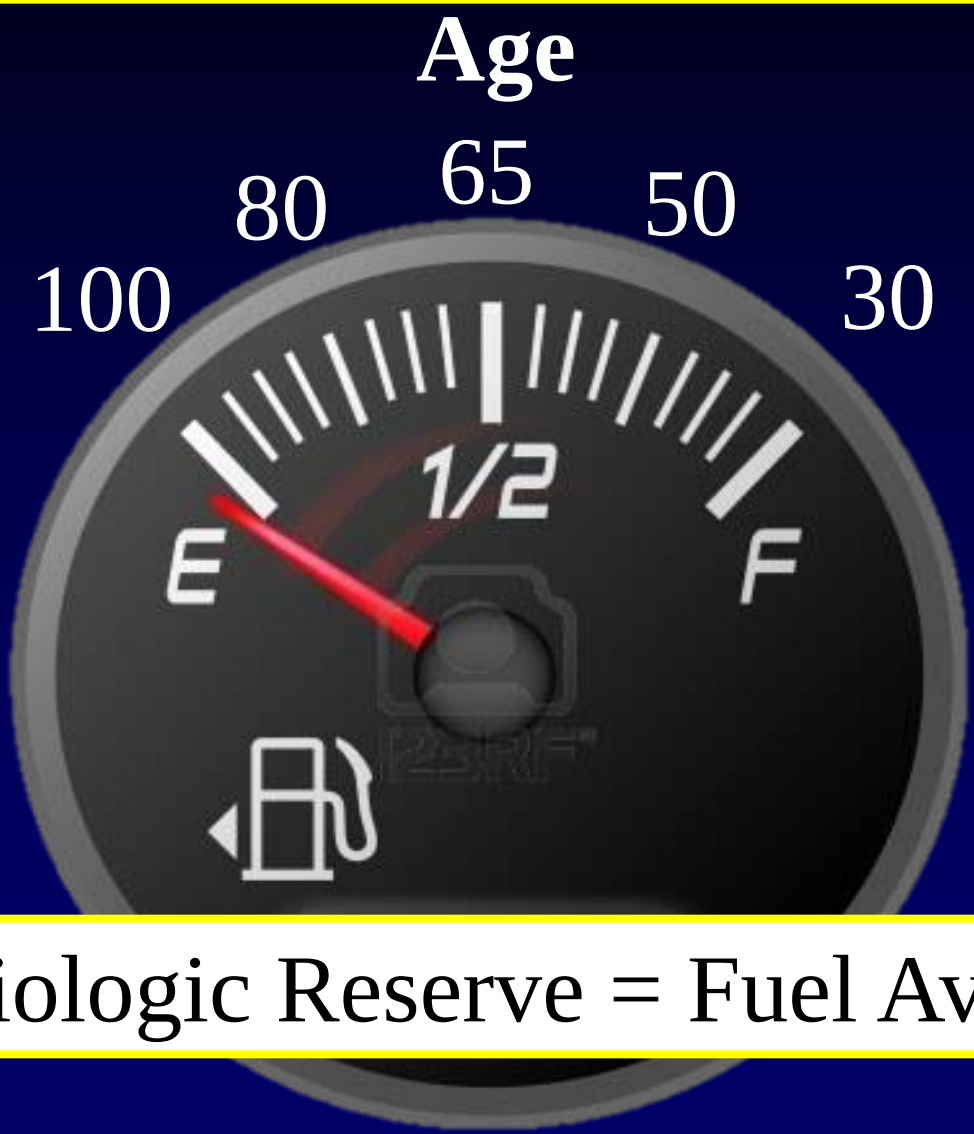
The Older Patient: Key Questions Not Addressed

- Do we need to treat the cancer?
  - Who will die of disease vs. with disease?
- If we treat, who is vulnerable to toxicity?
- How to modify therapy based on:
  - their organ function
  - their functional status
  - their cognitive status
  - their social situation

Aging

- Heterogeneous process
- Characteristic universal changes in physiology
- Affects each individual at a unique pace
- Depletion of physiologic reserve

Hallmark of Aging: Decreased Physiologic Reserve



Physiologic Reserve = Fuel Available

Determining Eligibility for Cisplatin

- Methods:
  - Survey of 120 oncologists specializing in urothelial cancer
  - Review of published literature on ineligibility for cisplatin

↓

Consensus definition of unfit patients for cisplatin-based therapy

- WHO/ECOG PS of 2
- CrCl < 60 mL/min
- Grade ≥ 2 hearing loss (~25 db)
- Grade ≥ 2 peripheral neuropathy
- NYHA class III heart failure

Age alone should not be used to classify unfit patients in clinical trials

Galsky, Lancet Oncol, 2011

Key Organ Function Considerations in Urothelial Cancer

- Renal Function
- Cardiovascular Changes
- Neuropathy
- Ototoxicity
- Bone Marrow Toxicity

Decline in Organ Function Not Obvious

Renal Function Decreases with Aging

Age	Creatinine (mg/dL)	CrCl* (ml/min)
40	1.4	79
50	1.4	71
60	1.4	63
70	1.4	55
80	1.4	47
90	1.4	39
100	1.4	32

Creatinine: Not an adequate measure of renal function

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
Wright	Accurate in patients with GFR > 50

None are perfect
All are better than creatinine alone

Hurria & Lichtman, BJC 2008

Cardiovascular Disease and Aging

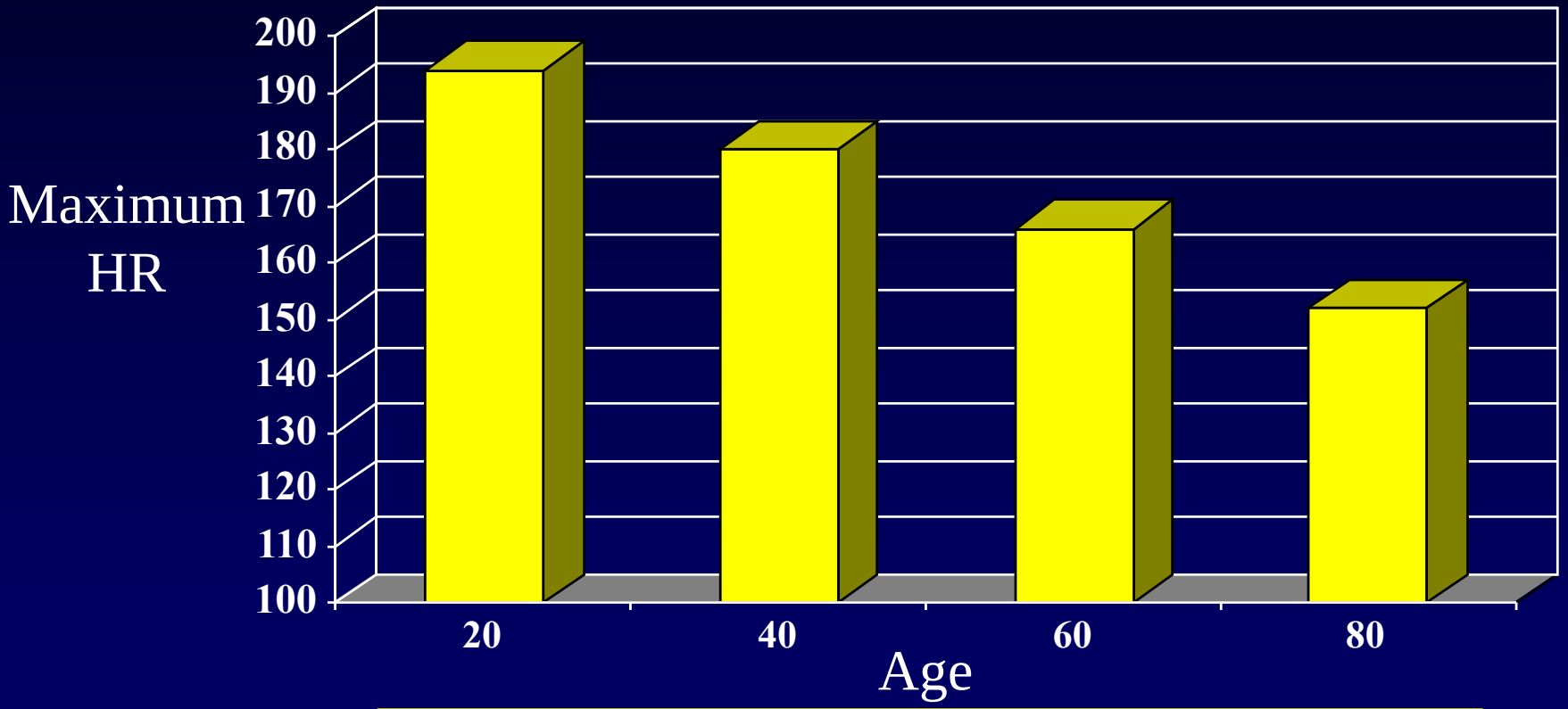
- Hypertension
  - Most common comorbid condition in older adults
  - 50-70% prevalence in age 65+
- Heart failure
  - Most common cause of hospitalization in age 65+

- Evaluate ejection fraction
- Avoid fluid overload
- Careful monitoring of I's/O's

Decline in Organ Function Becomes Apparent with a Stressor

Older Heart: Poorer Response to Stress

Decreased Maximum Heart Rate with Aging



Maximum HR = 208 – (0.7 x age)

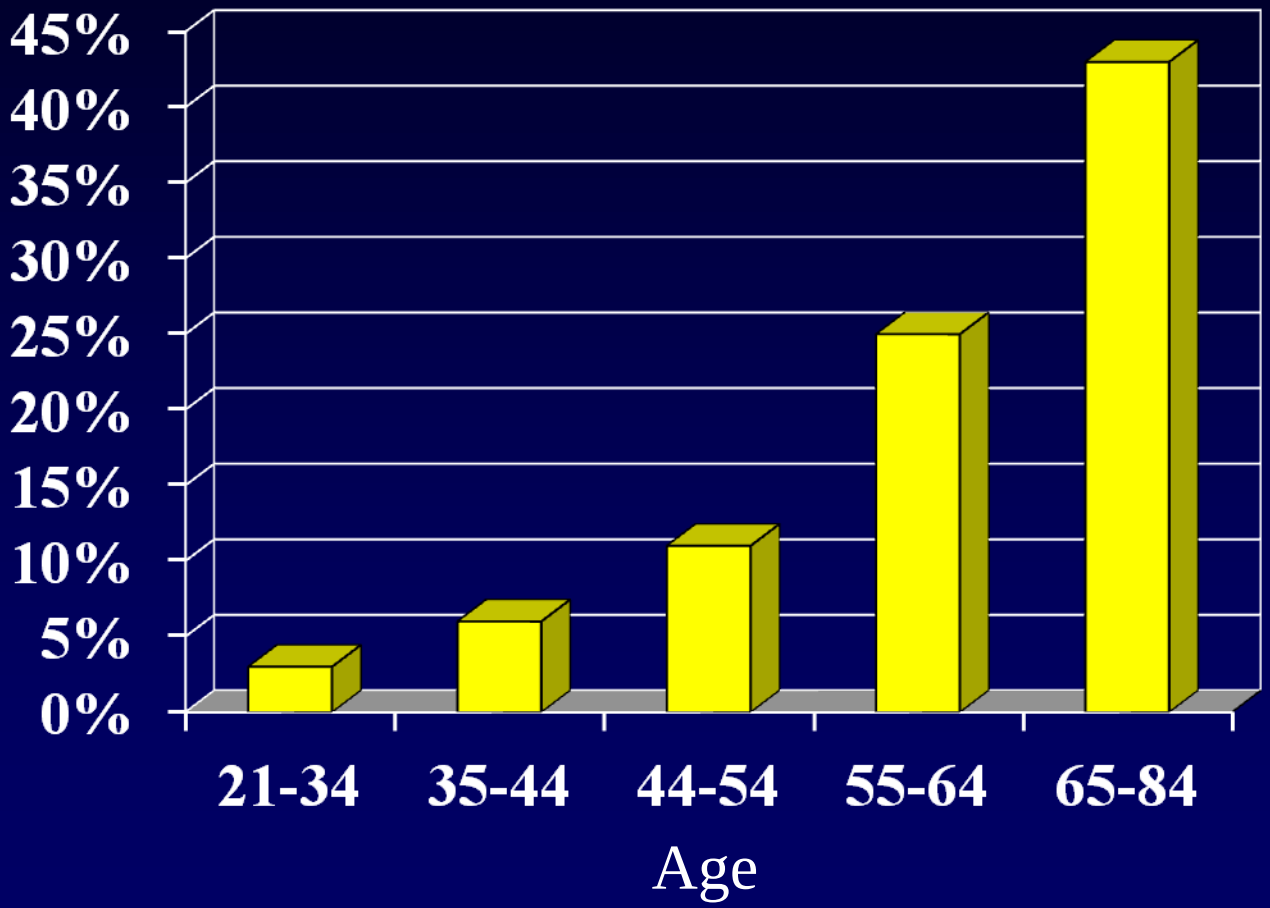
Tanaka, JACC 2001

Neurological Considerations with Platinum

- Neuropathy
  - Risk is associated with cumulative dose
  - Worsens in 30% after treatment is discontinued
- Ototoxicity
  - Systematic hearing loss 20%
  - Audiometric hearing loss 75%

Hearing Loss with Aging

- Presbycusis: “older hearing”



Nash, Arch Otolaryngol Head Neck Surg 2011

Bone Marrow and Aging

- Bone marrow reserve decreases with age
- Majority of death and serious infection occur in the 1st cycle
- NCCN guidelines:

  -Empiric growth factor for chemo of CHOP like intensity
- ASCO guidelines:

  -Empiric growth factor if febrile neutropenia rate > 20%

  -Older patients: population at risk

Gomez et al. JCO, 1998

Ozer et al, JCO, 2000

NCCN Guidelines® Myeloid Growth Factors, v2.2014

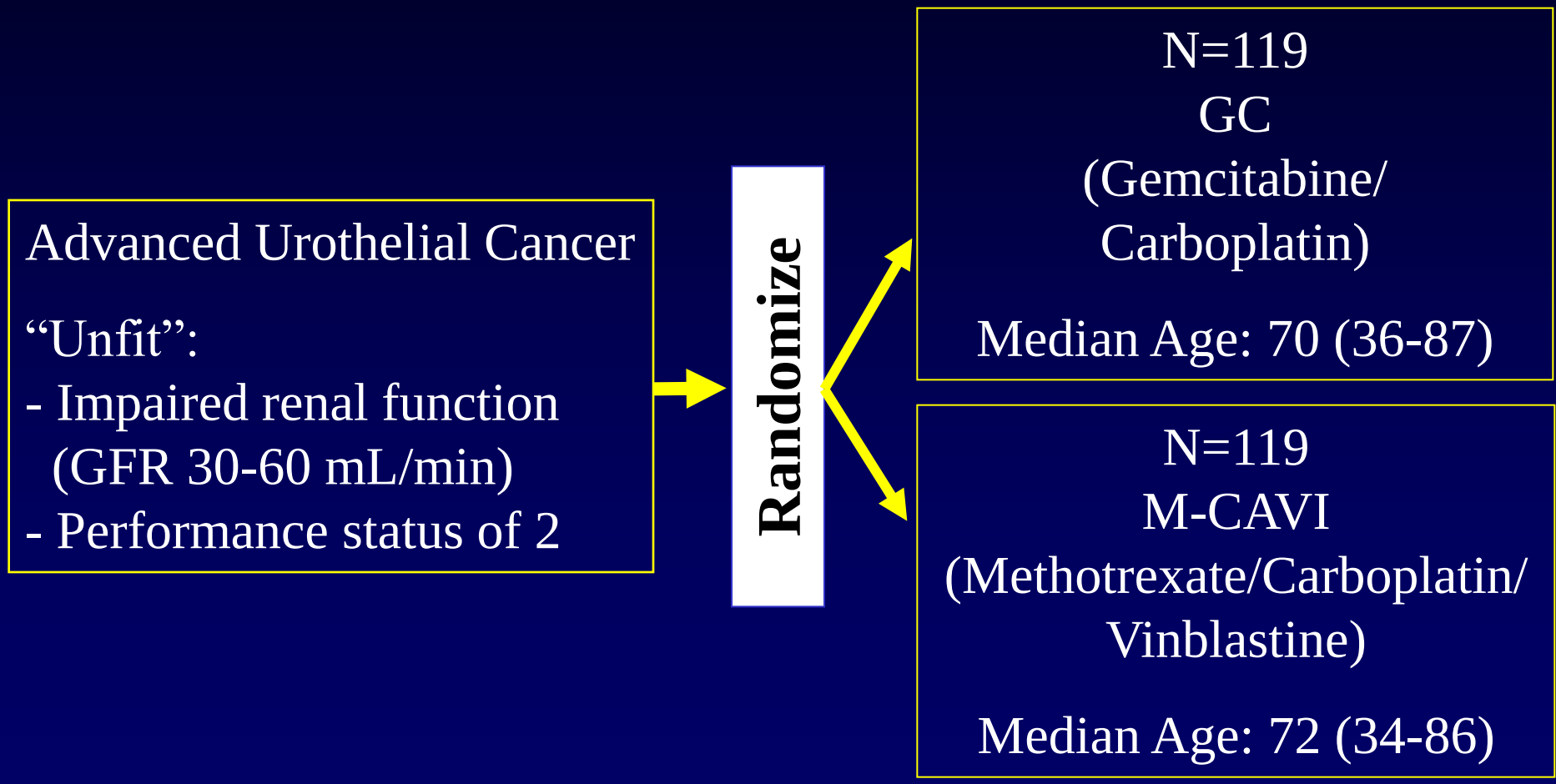
Smith et al. JCO, 2006

Chronological Age ≠ Functional Age

- Aging is heterogenous
- The aging trajectory is modifiable
- A hallmark of aging: decline in organ reserve
  - May not be obvious at rest
  - Becomes apparent with a stressor

Chemotherapy is a physiologic stressor
that can unmask the decline physiologic reserve

Treatment in Patients with Urothelial Cancer "Unfit" for Cisplatin-Based Chemotherapy EORTC Study 30986



De Santis, J Clin Oncol, 2009

EORTC Study 30986

Regimen	Complete/ Partial Response	Overall Survival	Severe Acute Toxicity	Toxic Death
GC	41.2%	9.3 mo.	9.3%	2.3%
M-CAVI	30.3%	8.1 mo.	21.2%	4.6%

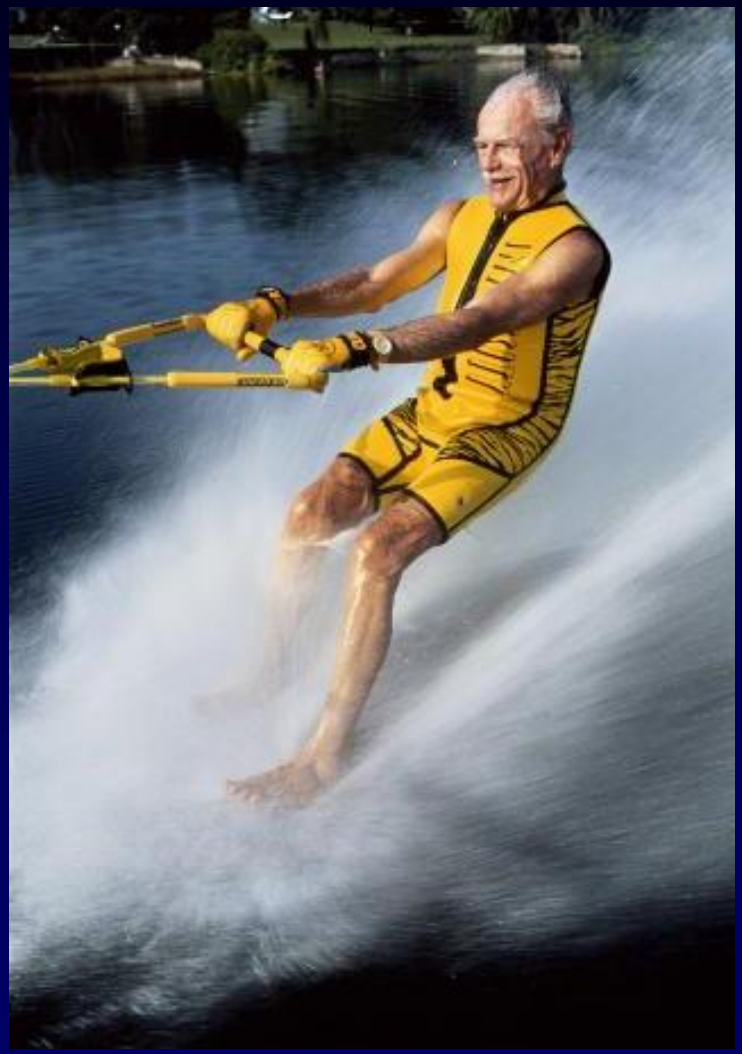
Conclusion:

- No difference in response or survival
- Decreased side effects with GC
- PS of 2 + GFR < 60 ml/min:
  - → 20% only received 1 cycle of tx
  - → 26% experienced severe toxicity

→ More clinical trials are needed

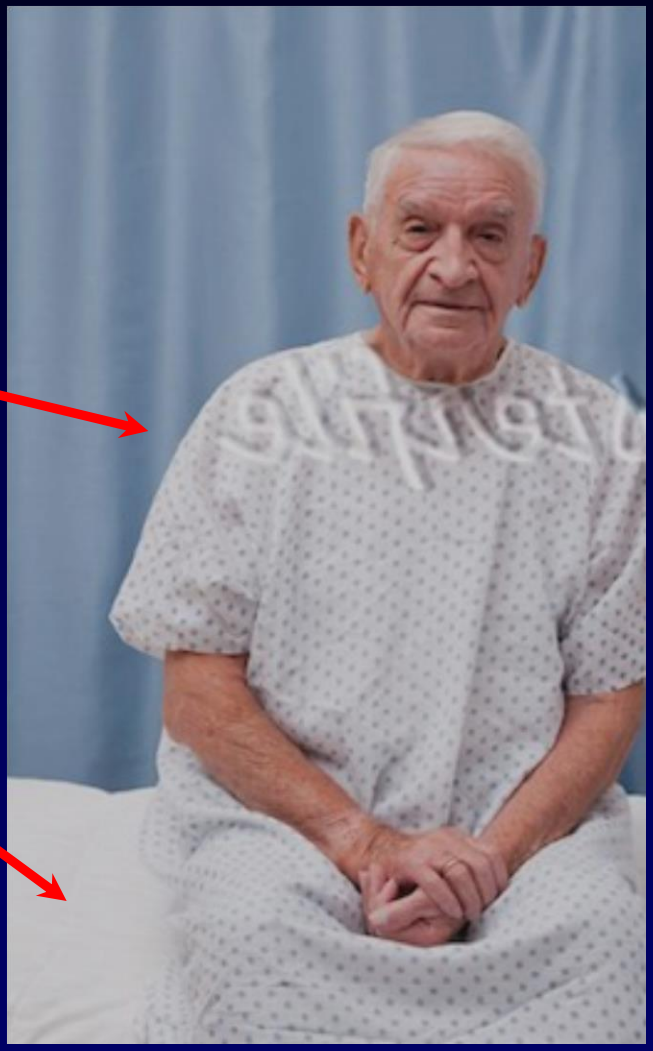
De Santis, J Clin Oncol, 2009

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



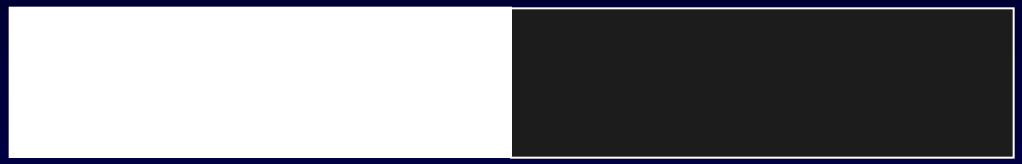
The Ultimately Efficient Clinic

- Vitals Taken
- Patient in Gown
- Sitting on Exam Table



What is old?

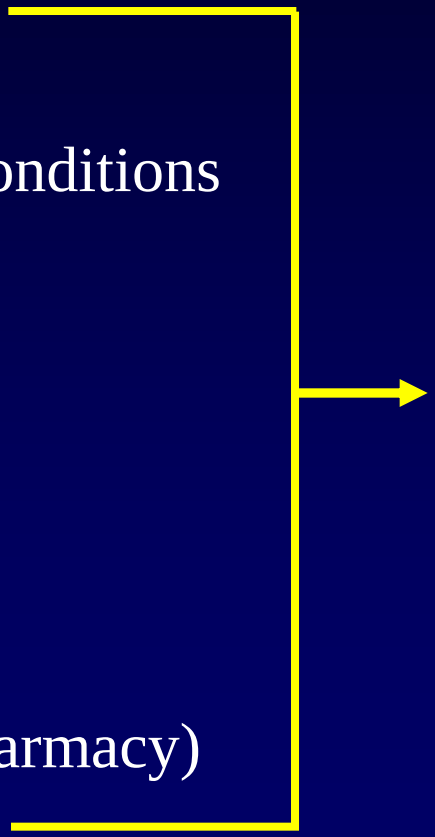
65



Integrating Geriatrics into Oncology

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

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



Geriatric Assessment

Developing a Geriatric Assessment for Oncologists

- **Functional Status:**
  Activities of Daily Living (subscale of MOS Physical Health)
  Instrumental Activities of Daily Living (subscale of the OARS)
  Karnofsky Performance Rating Scale
  Timed Up & Go
  Number of Falls in Last 6 Months
- **Comorbidity:** Physical Health Section (subscale of the OARS)
- **Cognition:** Blessed Orientation-Memory-Concentration Test
- **Psychological:** Hospital Anxiety and Depression Scale
- **Social Functioning:** MOS Social Activity Limitations Measure
- **Social Support:**
  MOS Social Support Survey: Emotional and Tangible Subscales
  Seeman and Berkman Social Ties
- **Nutrition:**
  Body Mass Index
  % Unintentional Weight Loss in the Last 6 Months

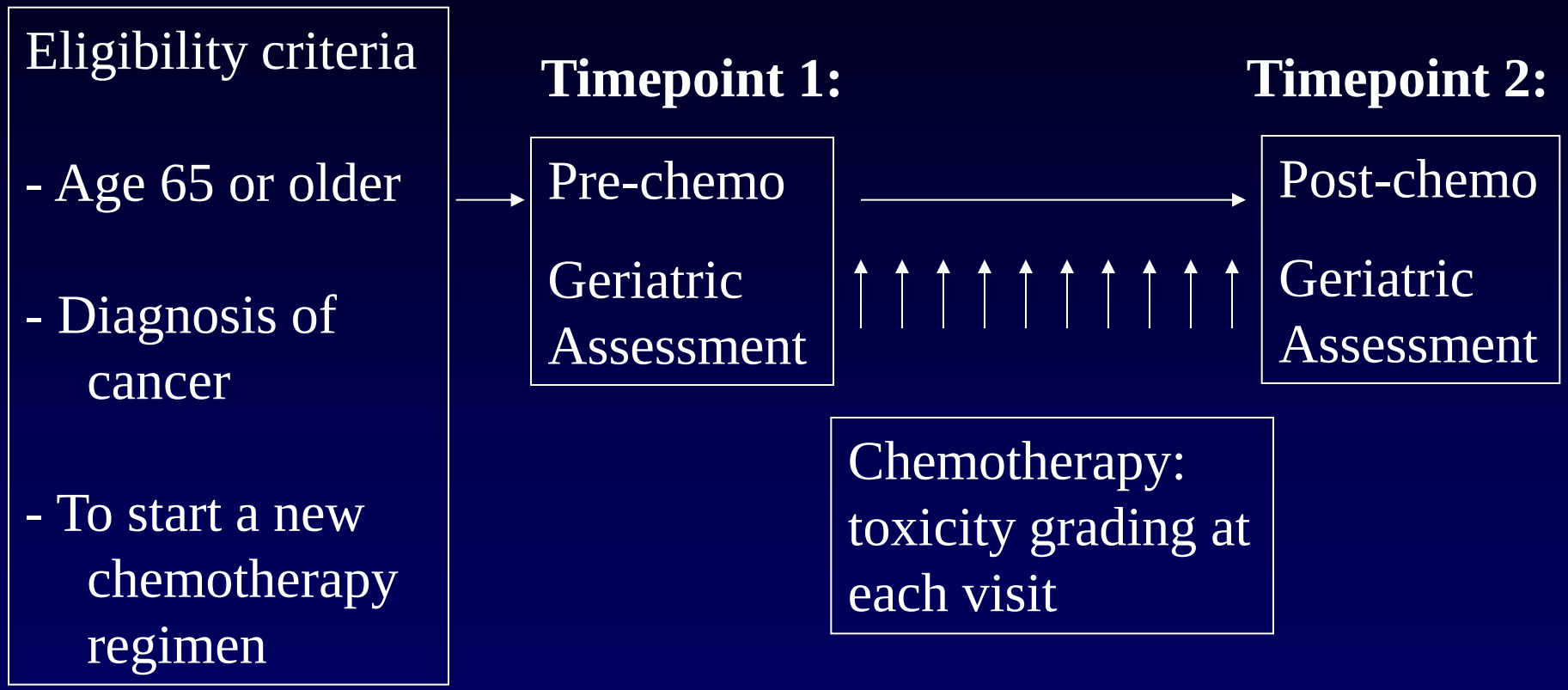
-Validity

-Reliability

- Length
- Time to complete
- Ability to self-administer

- Multidisciplinary input
- Alliance Cancer in Elderly Committee

Can Geriatric Assessment Predict Chemo Toxicity? (CARG)

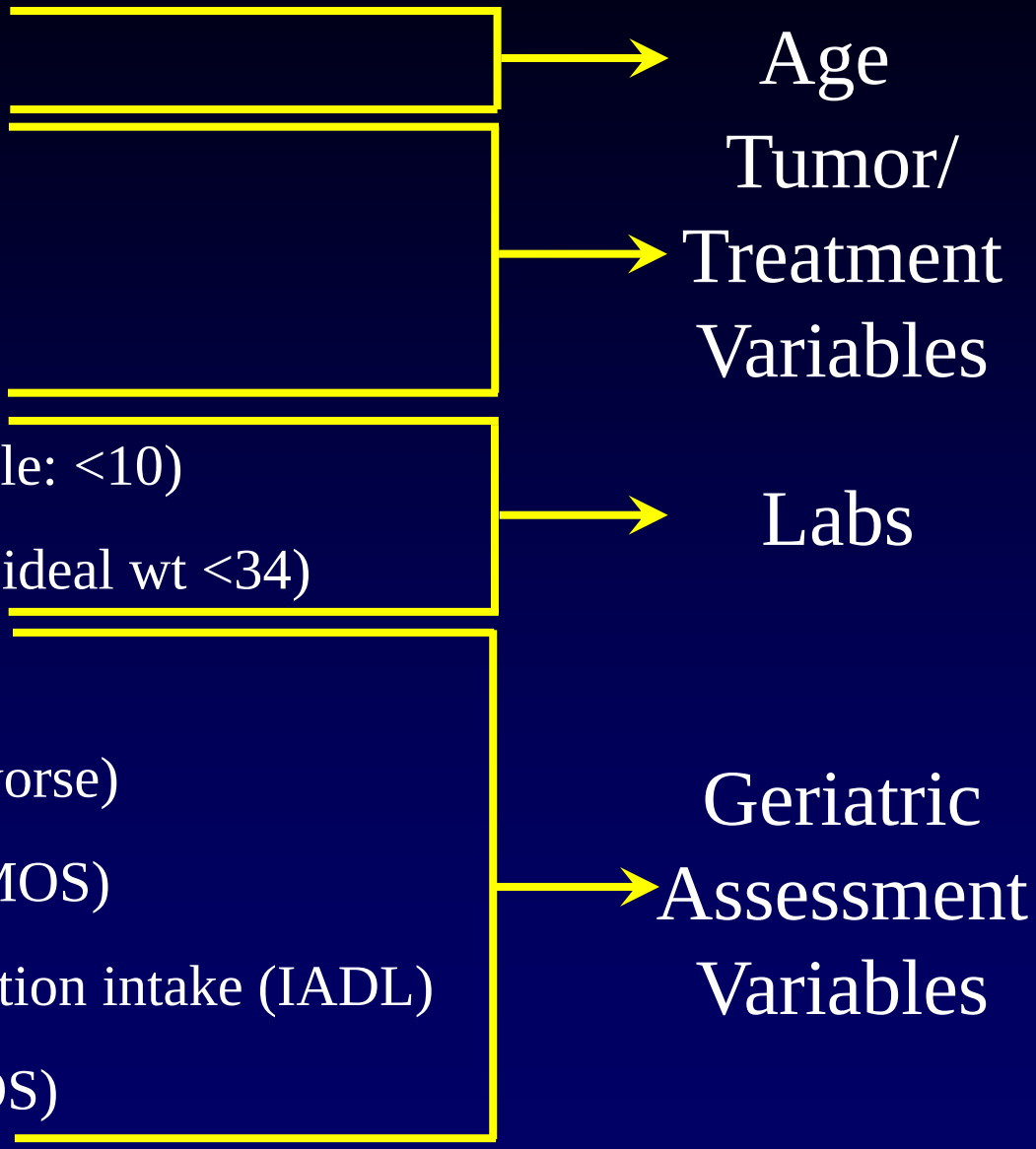


- Sample size: 500 patients (Chemo alone)
- 7 participating institutions (Cancer and Aging Research Group)

Hurria et al, JCO 2011

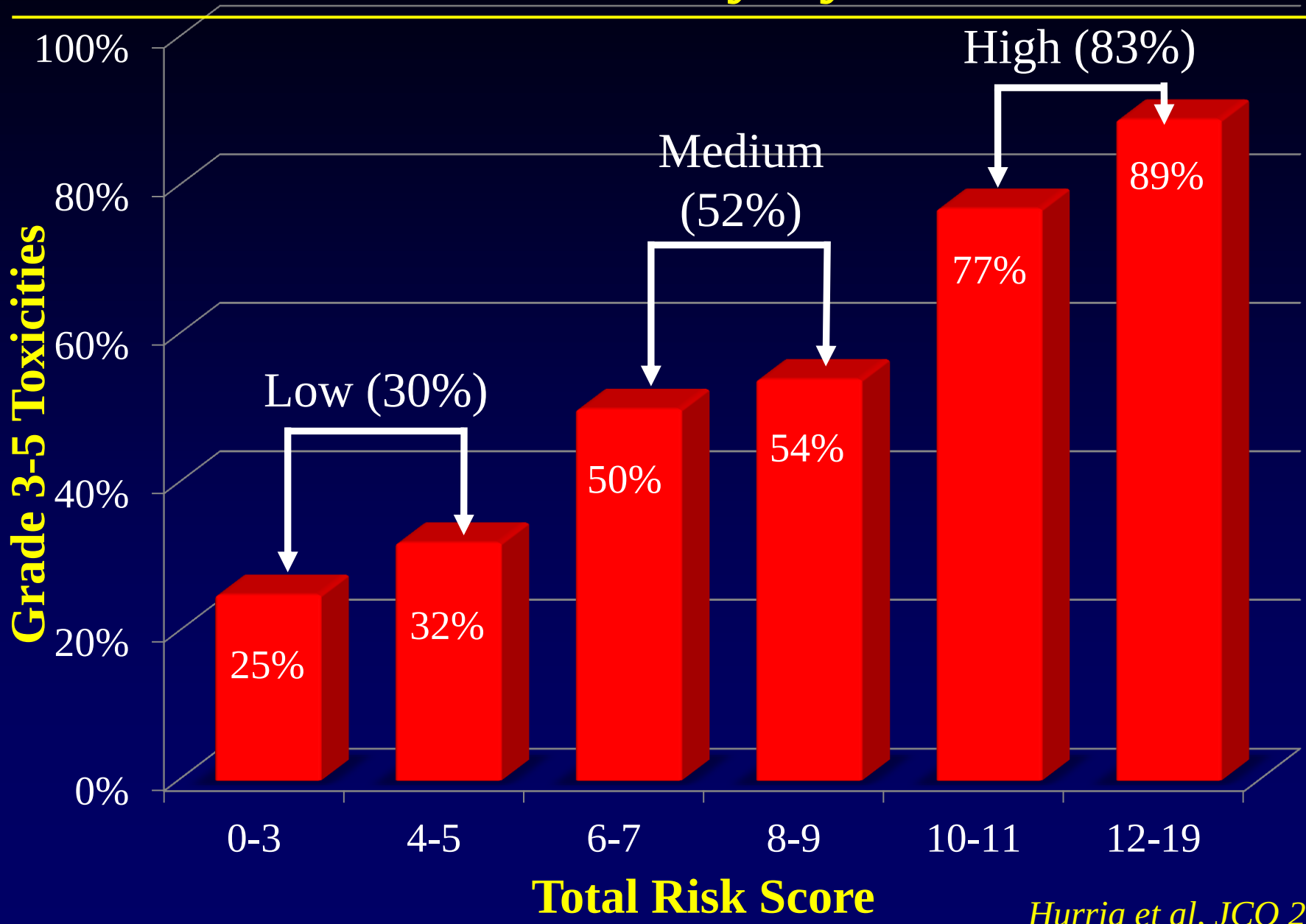
Predictors of Toxicity

- Age ≥ 72 years
- GI/GU Cancer
- Standard Dose
- Polychemotherapy
- Hemoglobin (male: <11, female: <10)
- Creatinine Clearance (Jelliffe-ideal wt <34)
- Fall(s) in last 6 months
- Hearing impairment (fair or worse)
- Limited in walking 1 block (MOS)
- Assistance required in medication intake (IADL)
- Decreased social activity (MOS)



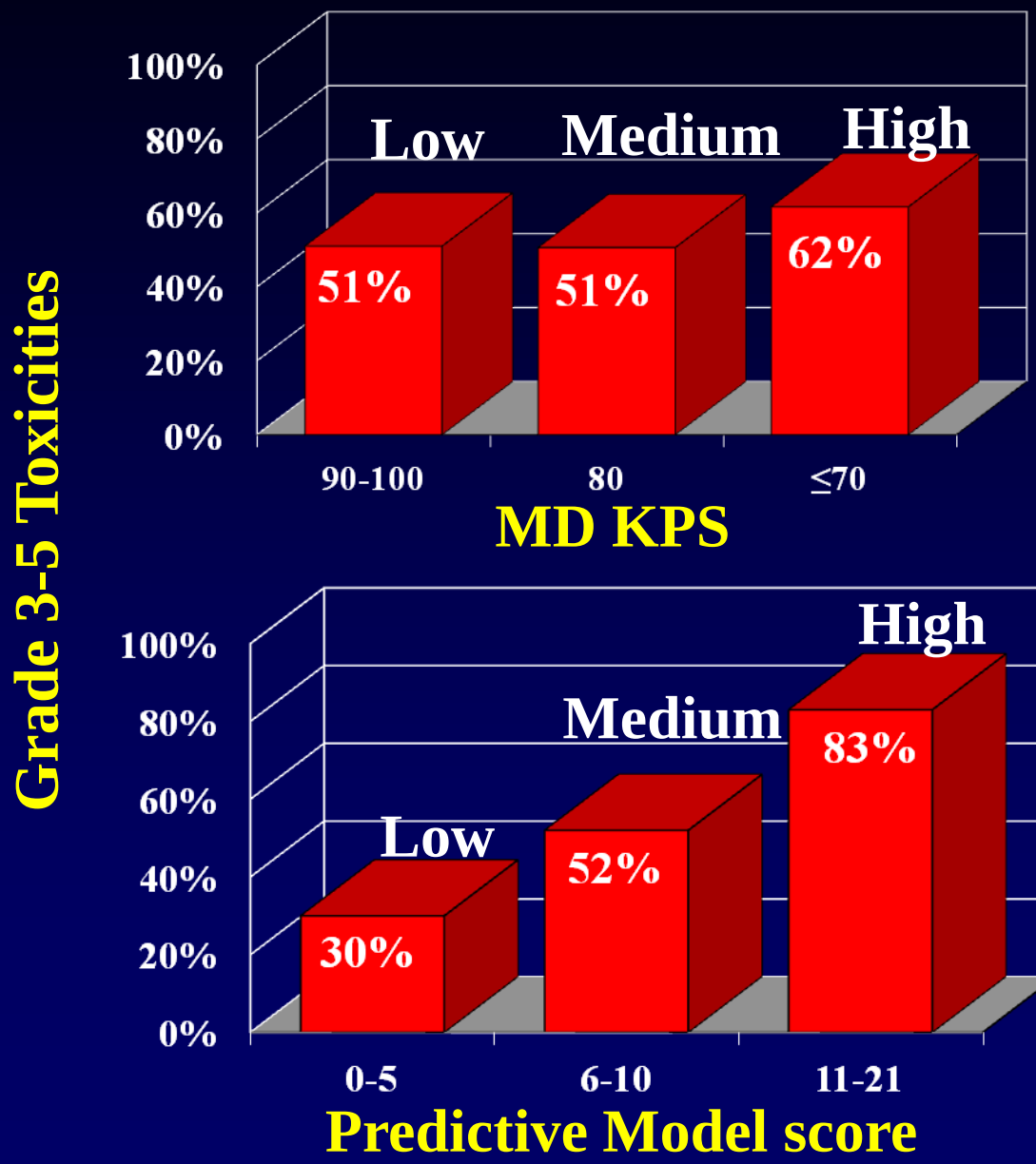
Hurria et al, JCO 2011

Risk of Toxicity by Score



Hurria et al, JCO 2011

MD-rated KPS vs. Predictive Model



Chi-square test $p=0.19$

Chi-square test $p<.0001$

Hurria et al, JCO 2011

Next Steps

- All Tumor Types: Validation Study
  - N=250; Completed Accrual
- Disease-Specific
  - Breast: Adjuvant Therapy (Dr. Hurria)
  - Ovarian: First Line Age ≥ 70 (Dr. VonGreunigan)
  - Breast: Endocrine Therapy +/- Bevacuzimab (Dr. Dickler)
  - Breast: Taxanes in Metastatic Breast Cancer (Dr. Rugo)
  - AML: First Line Age ≥ 60 (Dr. Klepin/Dr. Ritchie)
  - CLL: First Line Age ≥ 65 (Dr. Woyach)
  - GI: First Line Age ≥ 75 (Dr. McCleary)

The Past: Risk Factors for Chemotherapy Toxicity

- Patient Factors
  - Age
  - ECOG PS/KPS
  - Labs
- Tumor and Treatment Factors
  - Cancer Type
  - Chemotherapy

The Present: Geriatric Assessment Items Predictive of Chemotherapy Toxicity

Risk Factors	Aaldriks	Aparicio	Extermann	Freyer	Hurria	Kanesvaran	Soubeyran
Daily Activities (ADL & IADLs)		X	X	X	X	X	X
Hearing (Fair or Deaf)					X		
Nutrition	X		X			X	X
Cognition	X	X	X			X	X
Psychological Status	X	X		X		X	X
Social Activities					X		

Aaldriks et al, Crit Rev Oncol Hematol 2011
Aparicio et al, J Clin Oncol 2013
Extermann et al, Cancer 2012
Freyer et al, Annals of Oncology 2005
Hurria et al, J Clin Oncol 2011
Kanesvaran et al, J Clin Oncol 2011
Soubeyran et al, J Clin Oncol 2012

Tools are Available to Identify Older Adults at Risk & Guide Practical Interventions

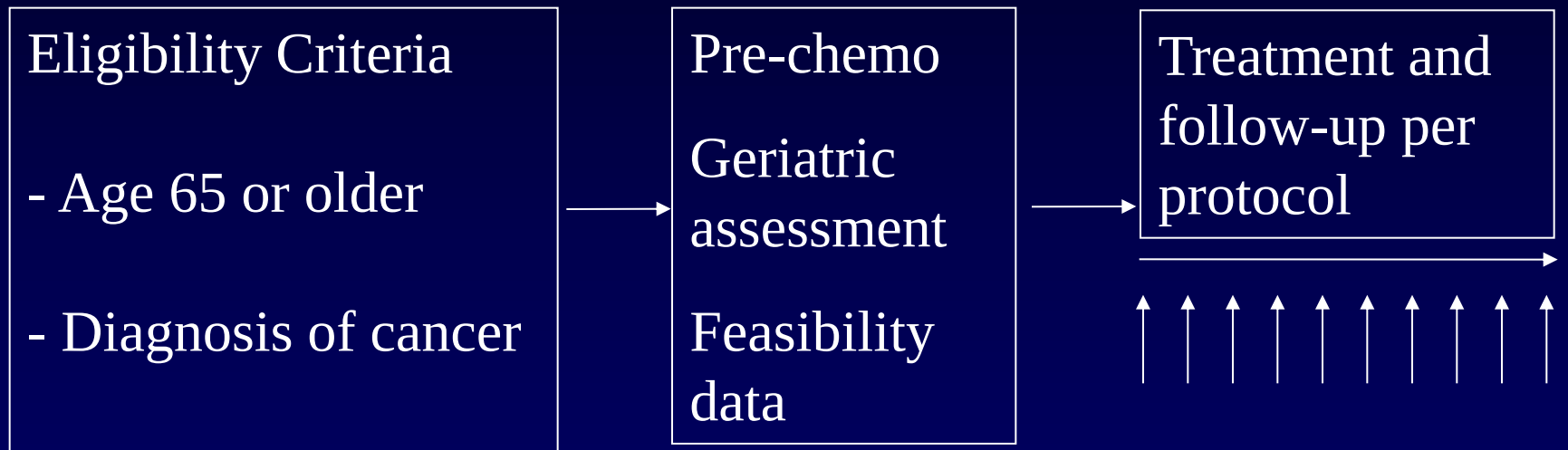
- Predict toxicity to cancer treatment
- Predict survival of older patients with cancer
- Uncover problems not detected by routine H&P
- Leads to practical interventions

Is it feasible to incorporate these tools into oncology practice?

Geriatric Assessment is Feasible

CALGB 360401 (PI: Hurria)

Primarily self-administered (Paper/Pencil)

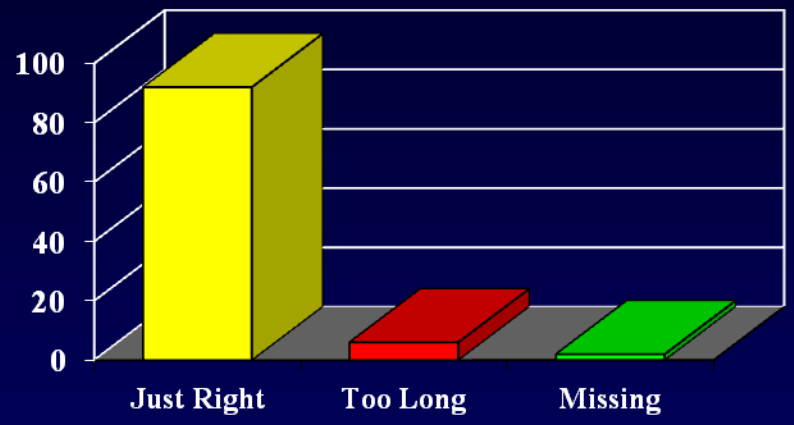


Geriatric Assessment is Feasible in Oncology Trials
(Time to Complete: Median 22 min.)

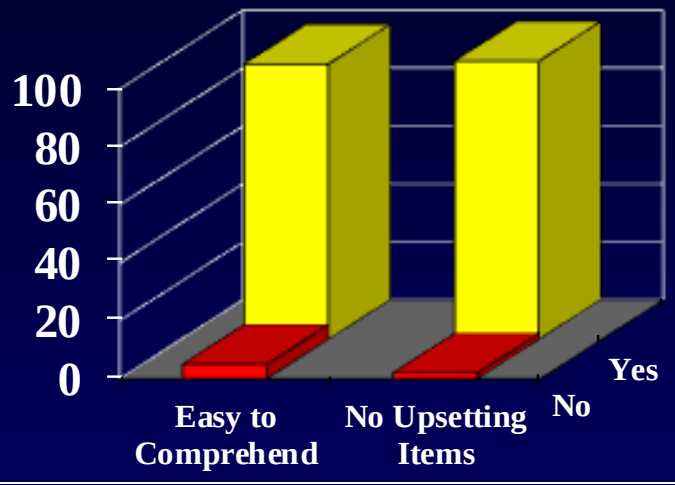
Hurria et al, JCO 2011

Geriatric Assessment Questions are Acceptable to Patients

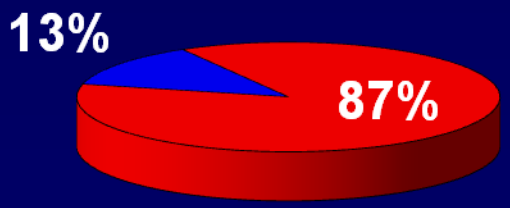
92% Length is "Just Right"



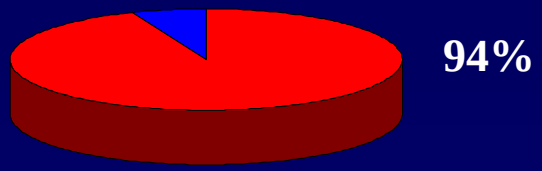
95% Easy to comprehend
96% Not upsetting



87% Completed patient questionnaire w/o assistance



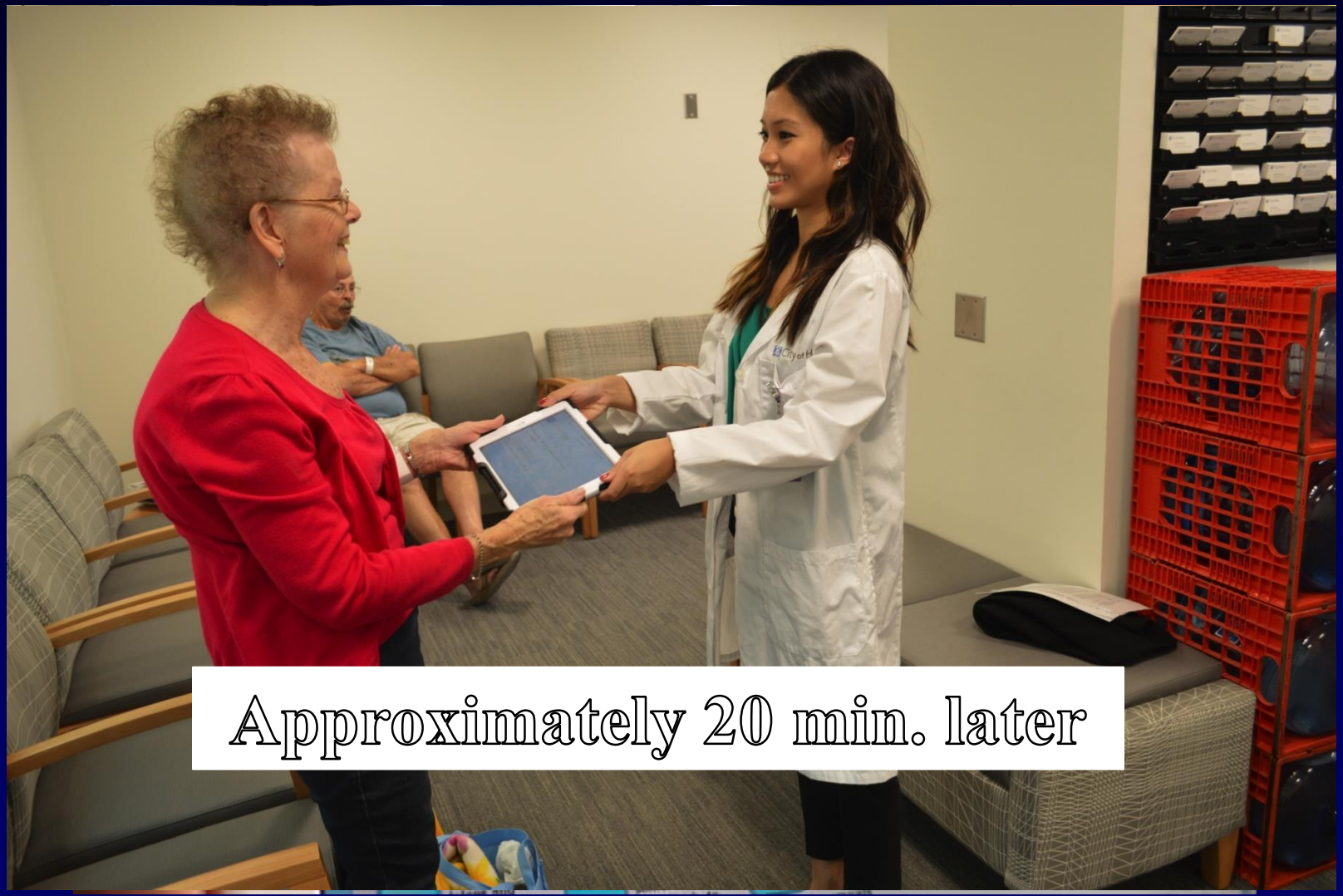
94% Completed healthcare provider portion



Hurria et al, JCO 2011

Facilitating Quality Cancer Care

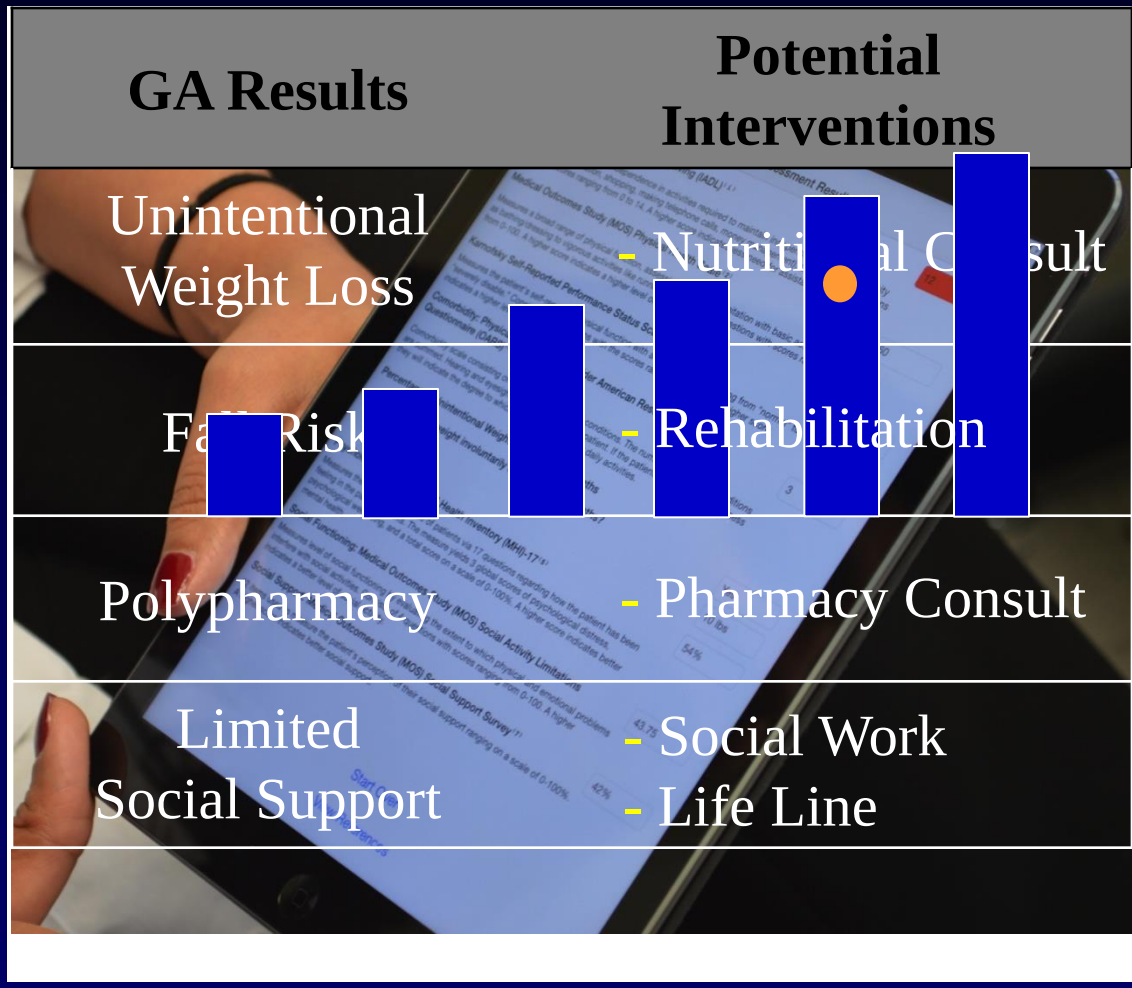
Everyone Completes a Geriatric Assessment



Facilitating Quality Cancer Care

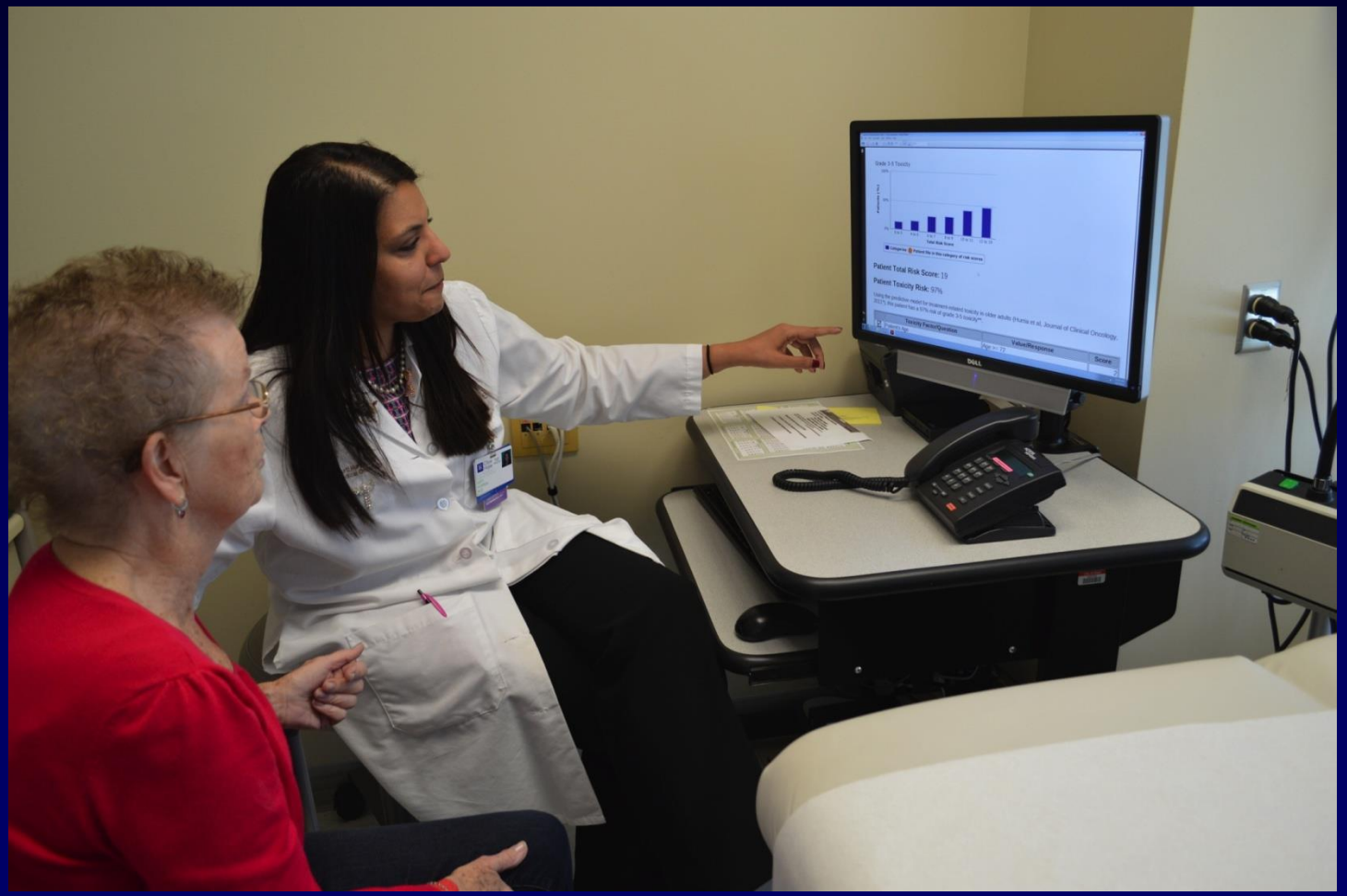
Information Provided to the Healthcare Team

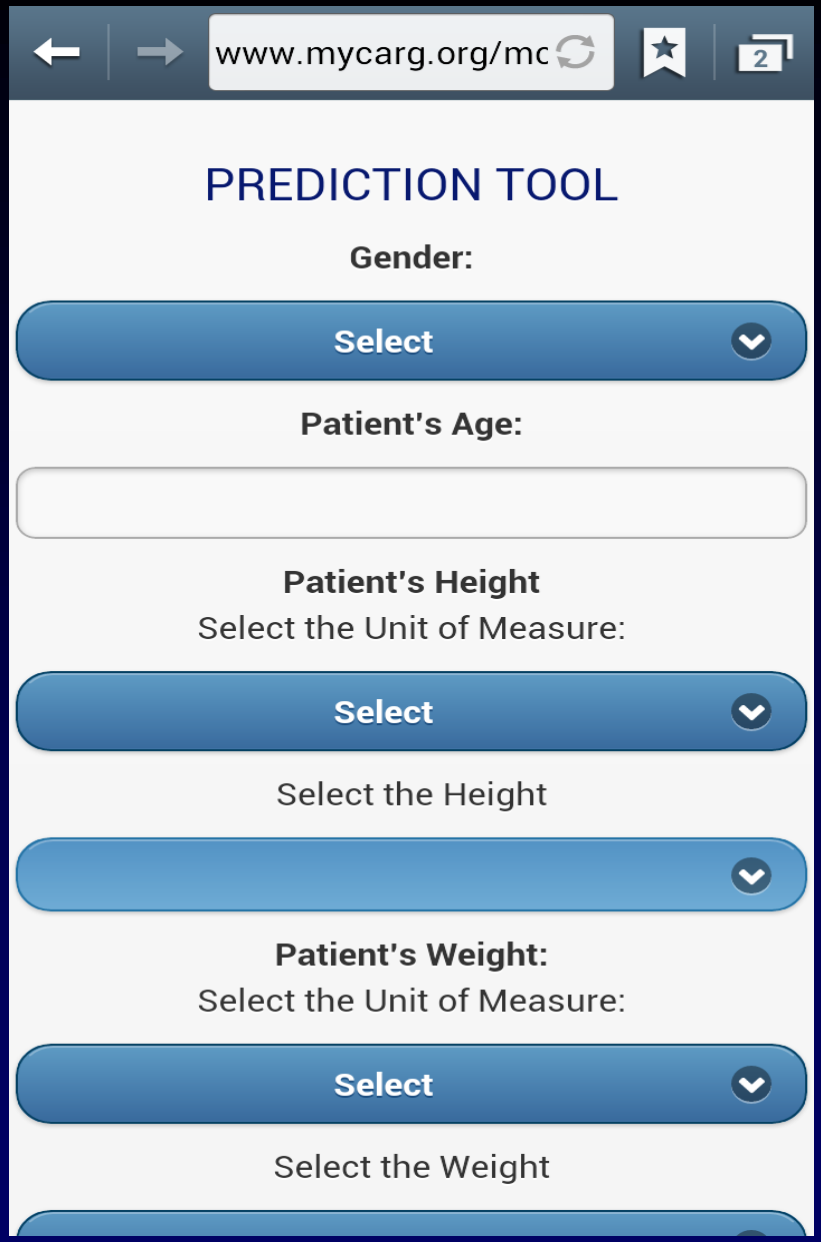
- Geriatric Assessment Results
- List of Potential Interventions
- Chemotherapy Toxicity Risk Score is Generated



Facilitating Quality Cancer Care

Facilitates Communication and Decision-Making Between the Oncologist and Patient





Submit

Creatinine Clearance:

44 **

Toxicity Score:

10

Risk of Chemotherapy Toxicity:

72%

What does this mean?

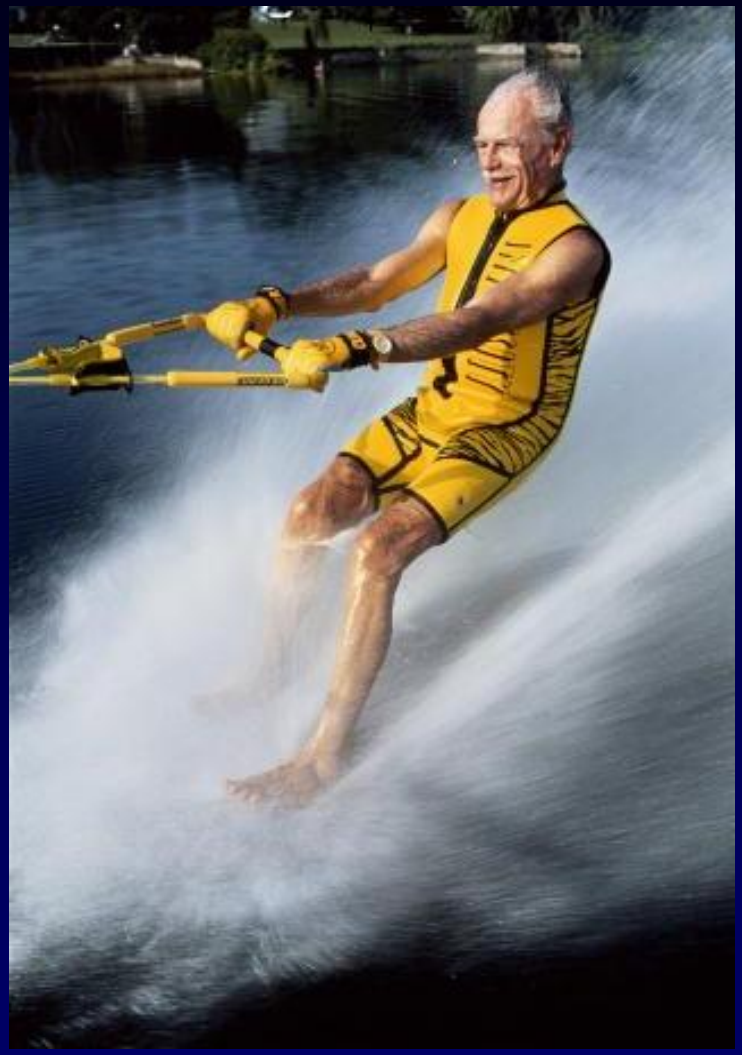
* Dose delivered with first dose for chemotherapy

** Jeliffe formula

http://www.mycarg.org/mctc

Chronological Age 80

Functional Age 90



Functional Age 60

Conclusions

- The population is aging
- Cancer is a disease associated with aging
- Aging is a heterogeneous process
- Organ function declines with aging
- “Chronological age” $\neq$ “functional age”
- Clinical trials in older adults are needed
  - Requires a melding of geriatric and oncology principles

Thank you!