Removing Barriers and Myths in Geriatric Oncology

Thomas Reske, M.D. PhD CMD FACP AGFS
Louisiana State University
Health Science Center
New Orleans, LA

UMC
UNIVERSITY
MEDICAL CENTER
NEW ORLEANS

LSUHealthNewOrleans
HEALTH SCIENCES CENTER

Geriatric Oncology

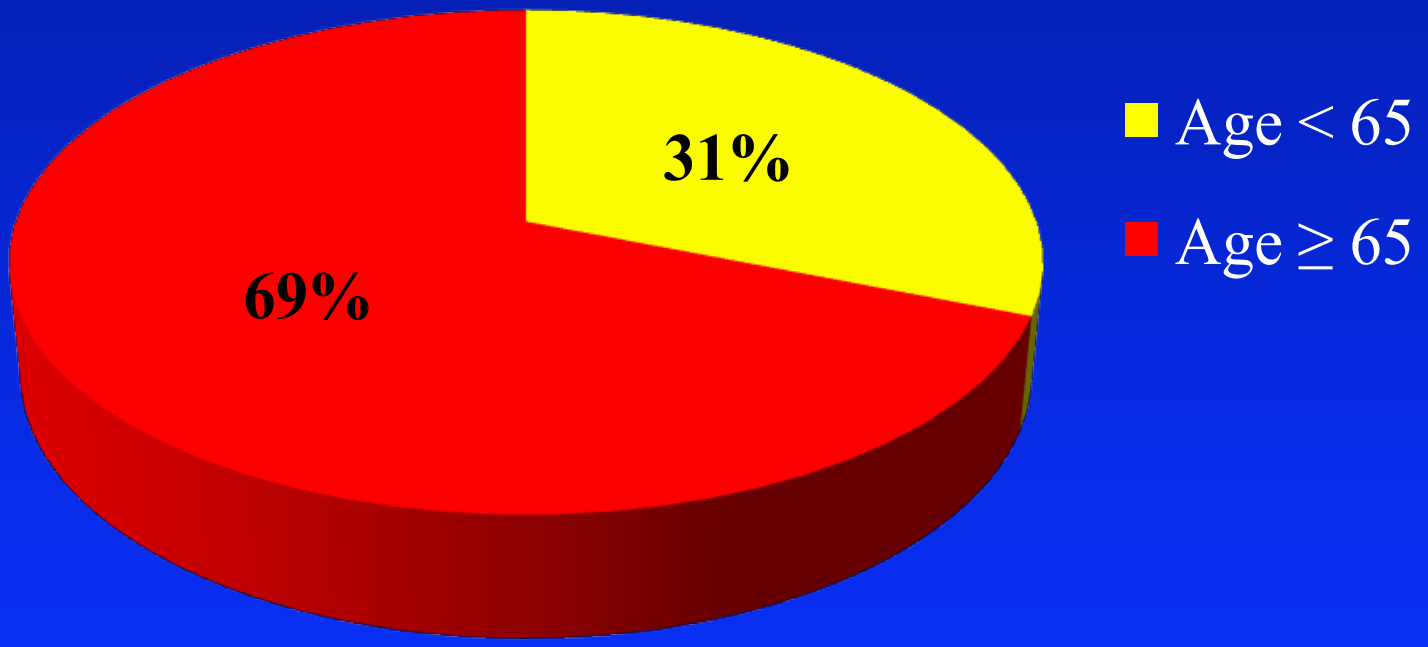
- Definition
- Epidemiology
- Pathophysiology
- Future direction

Epidemiology

- Life-time risk to develop cancer 41%
- Cumulative risk increases to age 70
- 2010-2050 adults > 85 age is projected to grow from 5.5 to 19 Million

Am J Prev. Med 2014 March; 46 (3 01): S7-15

Cancer and Mortality



Majority of Cancer Deaths Occur in Older Adults

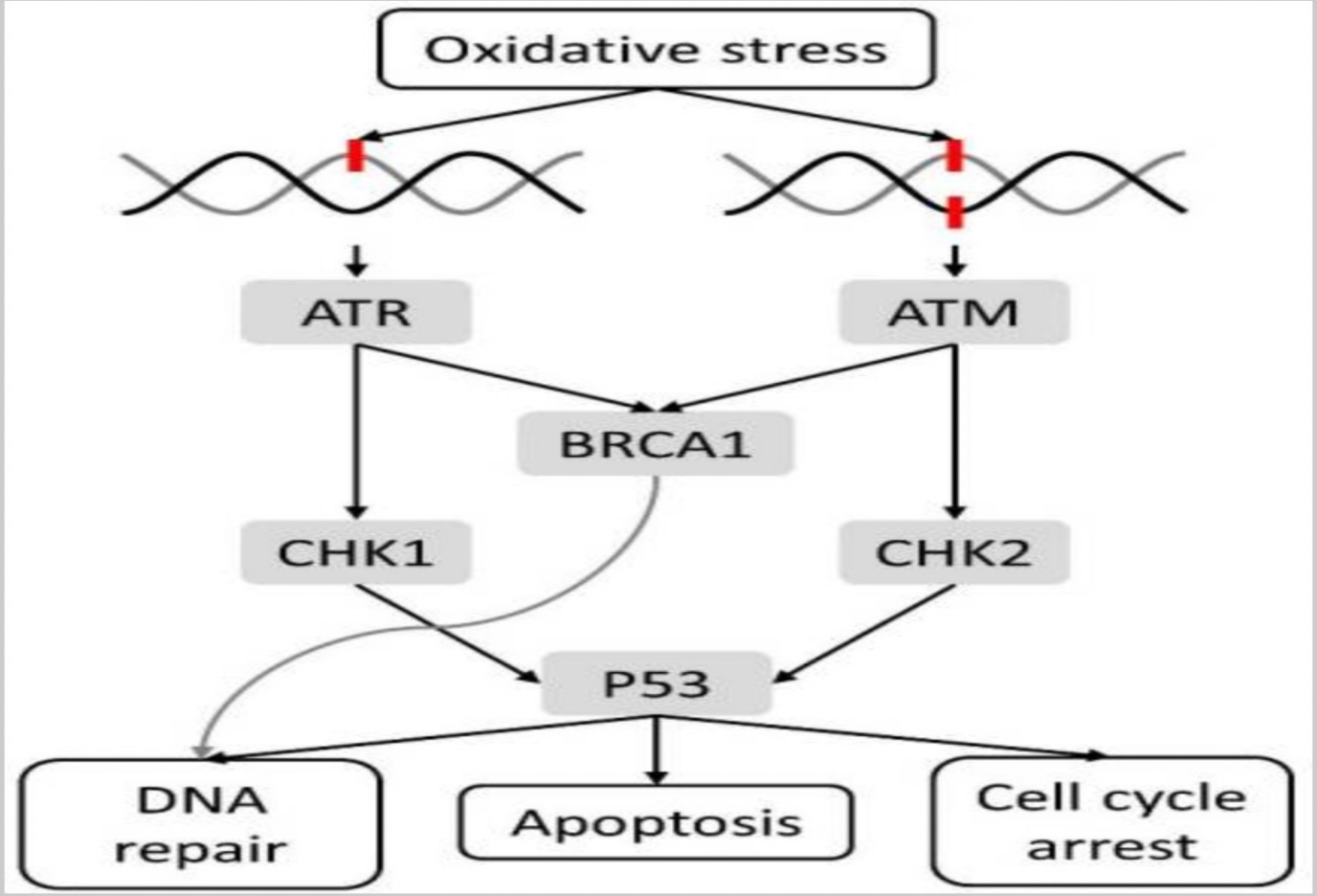
Howlader et al., SEER Cancer Statistics Review 1975-2010

Age is single
most important risk factor
to develop cancer

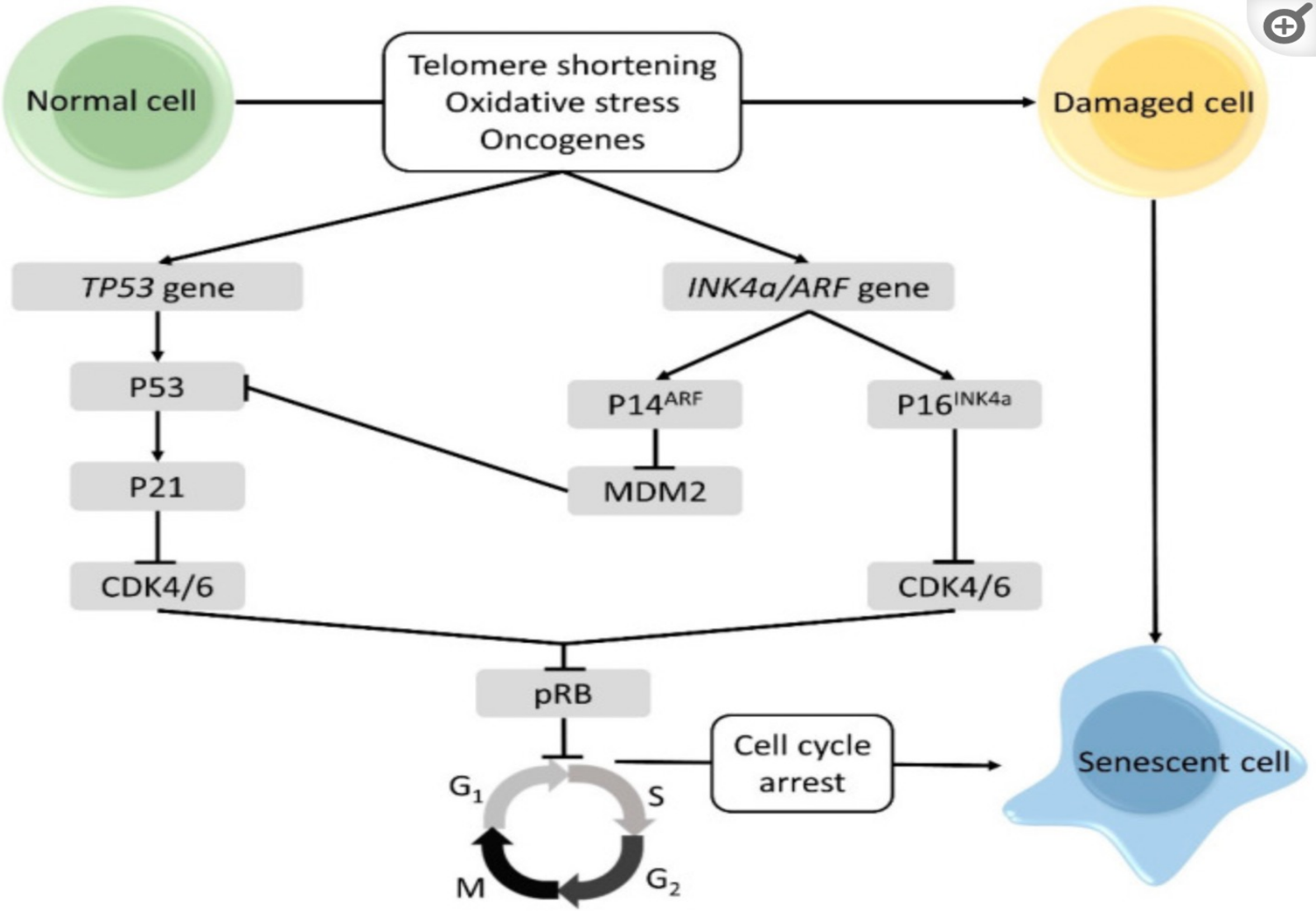
Pathophysiology

- Accumulation of oxidative stress and DNA damage over the years caused by a life-long exposure to endogenous metabolic insults (e.g., free radicals) and exogenous factors (e.g., UV irradiation, foods, etc.)
- Senescent cells accumulate during the aging process and exhibit a senescence-associated secretory phenotype (SASP)
- Progressive decay of immune function occurs in older individuals, whereby an effective immune response against developing tumors may fail

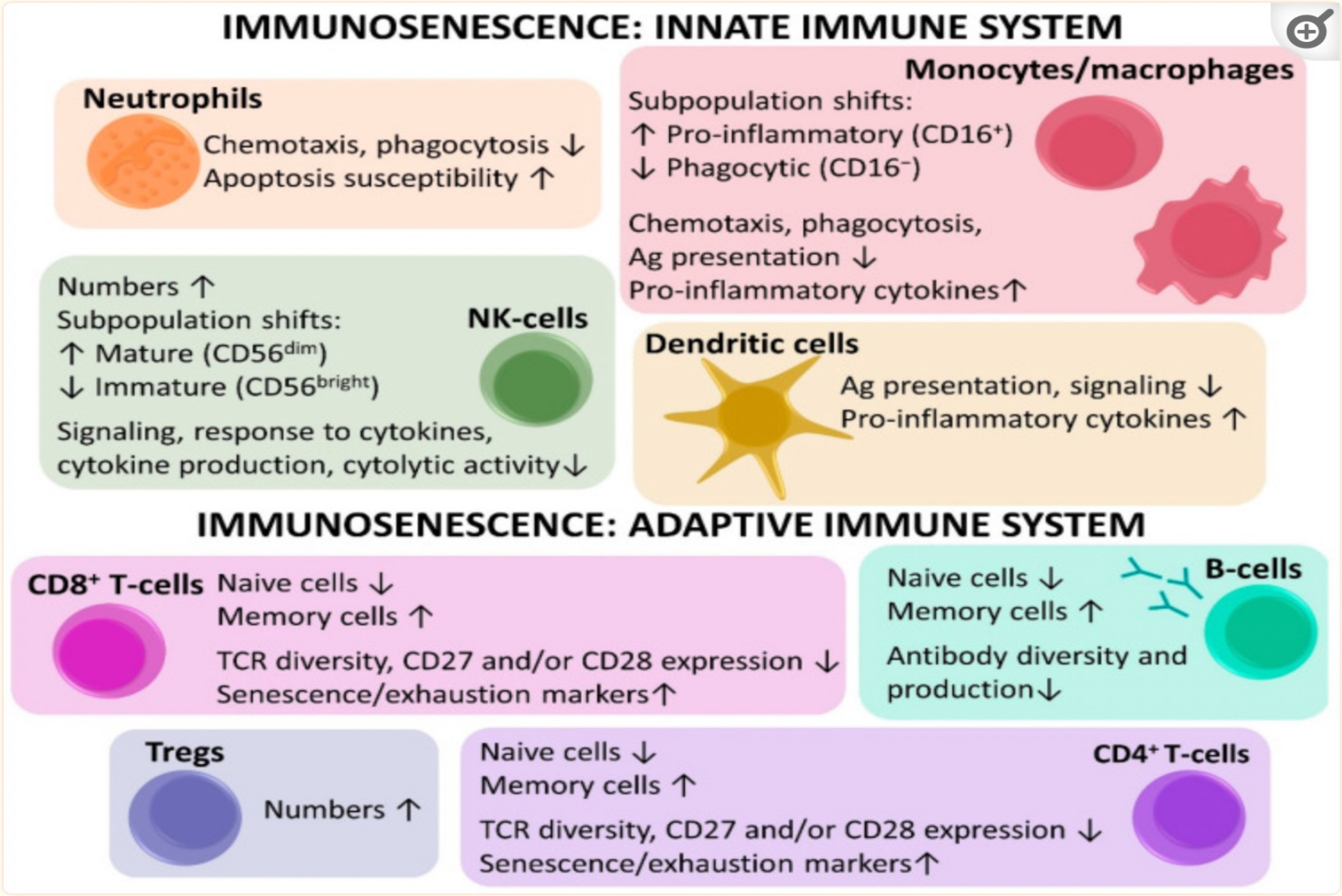
Cancers 2021 March; 13 (6): 1400



Cancers 2021 March; 13 (6): 1400



Cancers 2021 March; 13 (6): 1400



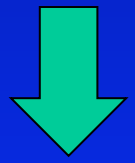
Cancers 2021 March; 13 (6): 1400

Importance

- Biological characteristics of certain cancers and their responsiveness to therapy may be different compared to their younger counterparts
- Psychological and psychosocial changes may impact an older-adults ability to tolerate cancer therapy
- Advanced age alone should not be the only criterion to preclude effective therapy that could improve quality of life or lead to a survival benefit in older patients

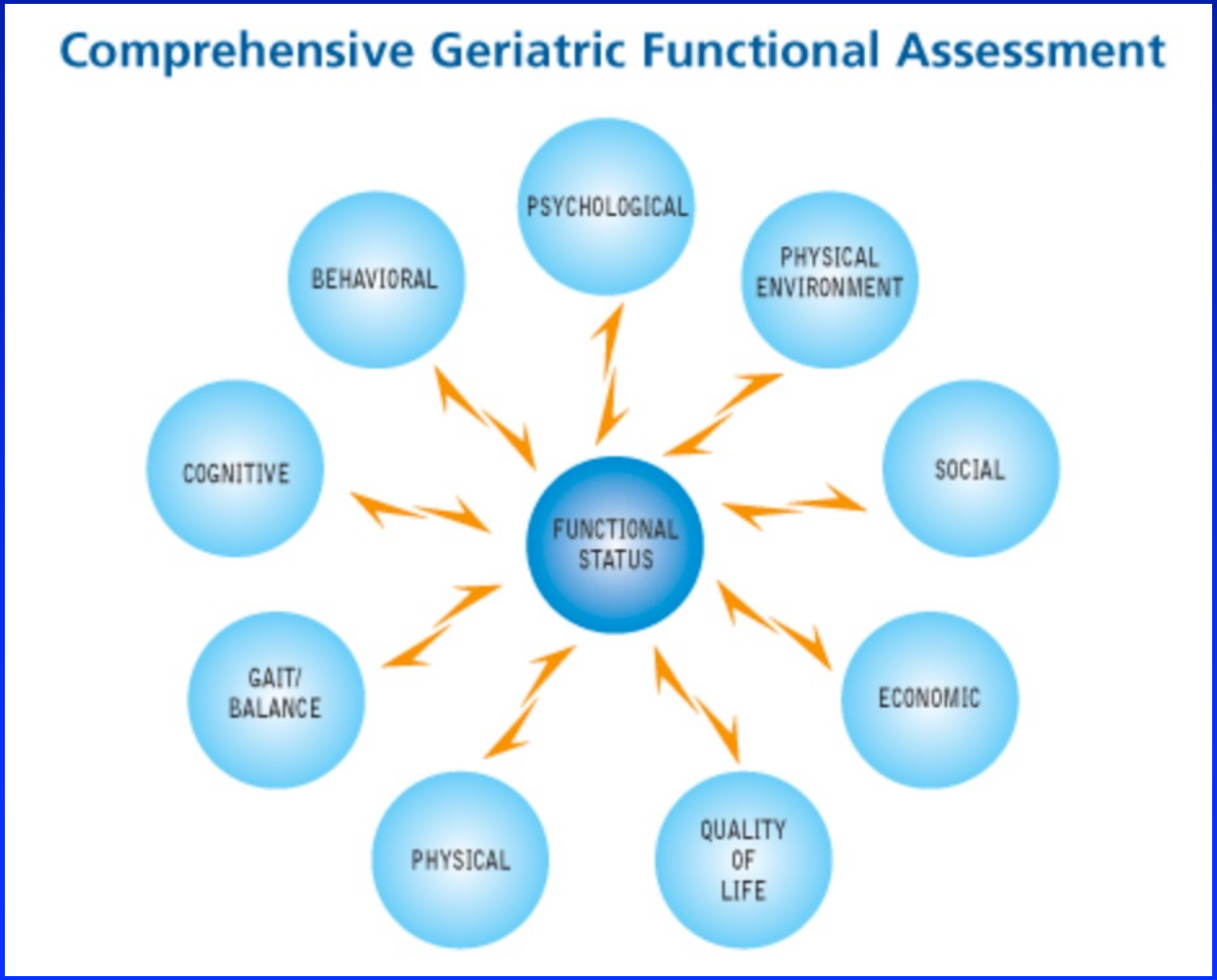
Common Misperception

- Neither chronological age alone nor performance status does justice to characterizing this heterogeneity



Tailoring treatment to the individual requires weighing risks against benefits in the context of frailty. It improves prognostication, risk stratification and communication with patients & caregivers, guide treatment adaptations, and provide non-oncologic interventions to increase resilience

KEY CONCEPT

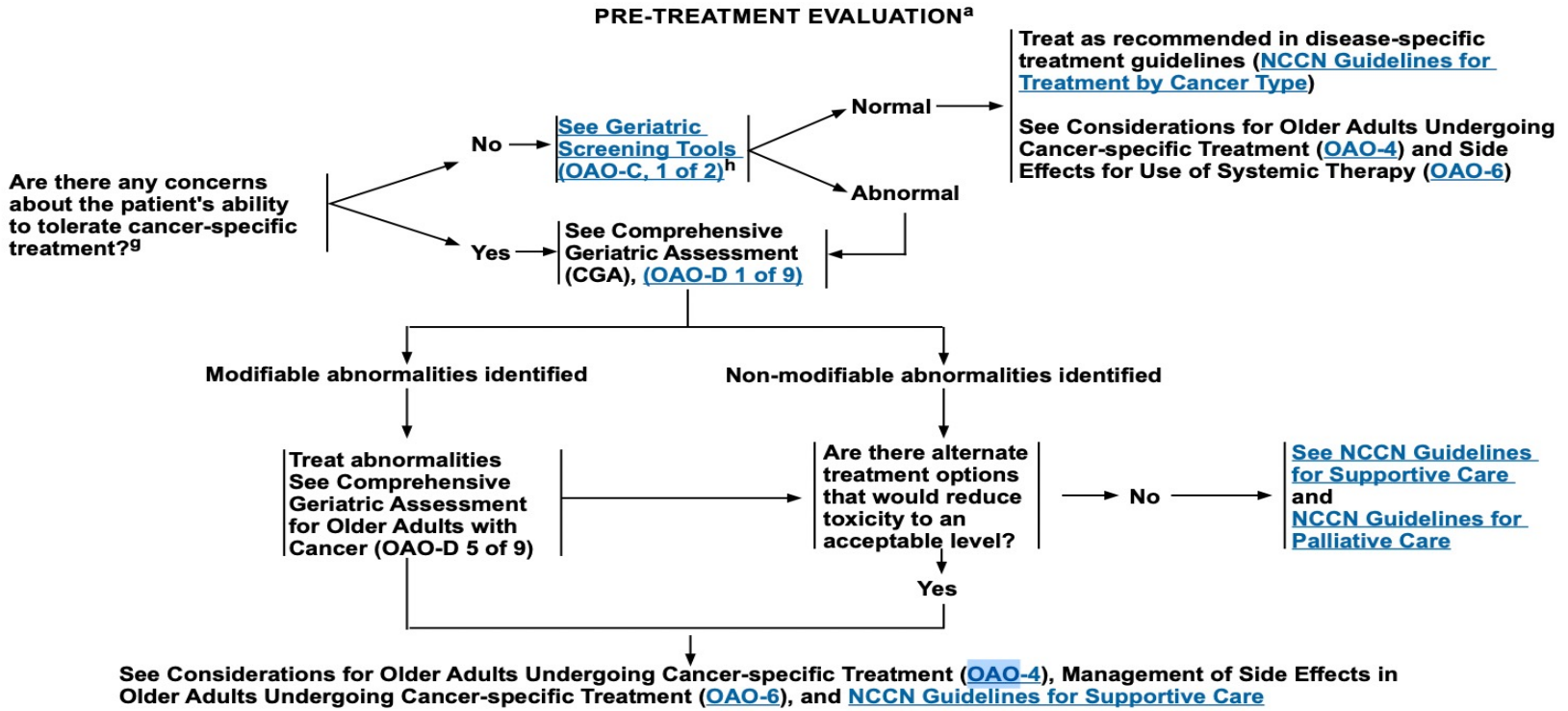

Comprehensive Geriatric Functional Assessment
PSYCHOLOGICAL
BEHAVIORAL
PHYSICAL ENVIRONMENT
COGNITIVE
SOCIAL
FUNCTIONAL STATUS
GAIT/ BALANCE
ECONOMIC
PHYSICAL
QUALITY OF LIFE

Comprehensive Geriatric Assessment

- Can detect reversible geriatric problems not found on routine exam
- Can predict toxicity, enabling more targeted use of supportive care measures
- Can help estimate life expectancy, important for making treatment decisions
- Allows for targeted interventions, which can improve QOL and adherence to therapy
- Can help improve communication

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2022
Older Adult Oncology



[a] Assessment of the patient's goals and objectives with regard to his/her cancer diagnosis should be completed prior to initiation of cancer-specific treatment. Supportive and palliative care assessment is recommended for any older adult with cancer (See OAO-2).

[g] Concerns can come from the patient, family, or clinician and can be related to the patient's performance status and/or comorbidities.

[h] Multiple screening tools have been tested and validated in this setting. Selected geriatric screening tools that have been used to determine if a CGA would be beneficial for older patients with cancer are listed on OAO-C, 1 of 2.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

OAO-3

Screening Tools

GERIATRIC SCREENING TOOLS

Abbreviated CGA (aCGA)[1,2]
Barber questionnaire[3]
Fried Frailty Criteria[4,5]
Geriatric (G-8)[6-8]
Groningen Frailty Index[2]
Triage Risk Screening Tool (TRST)[8]
Vulnerable Elders Survey (VES-13)[7,9-12]

Domains

- Self reported Function and Mobility
- Objective Function and Mobility
- Comorbidity
- Social Function and Support
- Cognition
- Psychological
- Nutrition
- Polypharmacy
- Fall

COMPREHENSIVE GERIATRIC ASSESSMENT (CGA)

Recommended Assessment Tools and Interventions for CGA of Older Adults with Cancer[a]

- CGA can be performed in a number of ways, the most extensive being with a geriatric trained clinician conducting a full assessment. Alternatively, there are tools that allow the clinician to perform these assessments within the oncology clinic setting as listed below.
- Patient's wishes/goals and objectives with regard to his/her cancer diagnosis should be assessed prior to any treatment decision. Supportive and palliative care assessment is recommended for all older adults with cancer. See NCCN Guidelines for Supportive Care and NCCN Guidelines for Palliative Care.

Domain	Assessment Tools[b]/Description	Potential Interventions
Self-reported Function and Mobility (OAO-D, 6 of 9)	Activities of Daily Living (ADLs) • Measures limitations in physical function activities, including bathing and dressing ▸ Katz Index of Independence in Activities of Daily Living (ADL)	• Physical medicine & rehabilitation referral • Occupational therapy referral • Home safety evaluation health care • Promote physical activity and exercise • Referral to geriatric trained clinical or primary care physician
	Instrumental Activities of Daily Living (IADLs) • Measures ability to complete activities required to maintain independence ranging from making telephone calls to money management ▸ OARS ▸ Lawton-Brody Instrumental Activities of Daily Living (IADL) Scale	
	Falls (See OAO-E) • Number of falls within the last 6 months	
Objective Function and Mobility (See OAO-E)	Time it takes for individuals to stand up, walk 10 feet, return to chair, and sit back down Timed "Up and Go" (TUG)	
	Assesses functional mobility Timed 10-Meter Walk Test	
	Short Physicial Performance Battery (SPPB) Evaluation of lower extremity functioning	

Adapted with permission from Mohile SG, Velarde C, Hurria A, et al. J Natl Compr Canc Netw 2015;13:1120-1130.
Abbreviations: OARS: Older Americans Resources and Services

[a] Completion of the proposed geriatric assessment will take an average of 20 minutes. Alternative tools that could be utilized are listed in the domain specific section.
[b] All of these assessments can be performed in less than 5 minutes.

MANAGEMENT OF SIDE EFFECTS IN OLDER ADULTS UNDERGOING CANCER-SPECIFIC TREATMENT[a]

Diarrhea	See NCCN Guidelines for Palliative Care
Constipation	See NCCN Guidelines for Palliative Care
Nausea/Vomiting	See NCCN Guidelines for Antiemesis and NCCN Guidelines for Palliative Care
Mucositis	• Early hospitalization is needed for patients with mucositis who also develop dysphagia/diarrhea. • Provide nutritional support. See NCCN Task Force: Prevention and Management of Mucositis in Cancer Care
Bone marrow suppression	(See NCCN Guidelines for Hematopoietic Growth Factors).
Neurotoxicity	• Monitor hearing loss and avoid neurotoxic agents if significant hearing loss is present. • Monitor cerebellar function if treated with high-dose cytarabine. • Monitor for peripheral neuropathy. • Monitor for cognitive dysfunction (See OAO-F).
Falls	• Periodic assessment of history of falls, balance, and gait difficulties is recommended for all patients as fall risk may change over time[8] (See OAO-E). • The use of early and preventive use of durable medical equipment and in-home safety evaluations is recommended for patients with neurotoxicities at high risk for falls.
Cardiac toxicity	• Monitor for symptomatic or asymptomatic congestive heart failure (CHF) ▸ Caution with use of anthracyclines; consider alternative treatment dosing schedule or treatment as appropriate per disease site (See NCCN Guidelines for Treatment of Cancer by Site) ▸ Caution with use of trastuzumab (among patients with normal left ventricular ejection fraction [LVEF], risk factors for CHF include older age, receipt of an anthracycline-based regimen, baseline LVEF of 50%–54%, coronary artery disease, hypertension, and weekly trastuzumab administration (See SCARDIO-1, SCARIO-2, SCARDIO-3 in NCCN Guidelines for Survivorship).[9,10,11]
Renal toxicity	• Serum creatinine is not a good indicator of renal function in older adults. Calculation of creatinine clearance is recommended to assess renal function and adjust dose to reduce systemic toxicity.
Insomnia (See OAO-H)	• Benzodiazepines or other sedative-hypnotics should not be used as first-line treatment for insomnia in older adults[12]; non-pharmacologic methods such as cognitive behavioral therapy and lifestyle modifications are preferred (See Sleep Disorders in NCCN Guidelines for Survivorship).

[a] Assessment of the patient's goals and objectives with regard to his/her cancer diagnosis should be completed prior to initiation of cancer-specific treatment. Supportive and palliative care assessment is recommended for any older adult with cancer (See OAO-2).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

GUIDELINES

- NCCN – Older Adults Oncology
- AGS – Geriatric Oncology Workgroup
- ASCO – Geriatric Oncology Resources
- SIOG - Clinical Practice Guidelines
- CARG – Cancer and Aging Research Group

Historic Development JCO Special Series

- 2007 Build evidence base in the field
- 2014 Clinical assessment and clinical trail design
- 2018 ASCO guidelines to risk stratify for chemotherapy toxicity
- 2021 Shift from GA risk assessment to GA interventions


Volume 39, Issue 19
July 1, 2021
Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal
SPECIAL SERIES
Caring for Older Adults With Cancer
Overview: Geriatric Oncology Comes of Age: Advancing the Science of Caring for Older Adults With Cancer. W. Dale et al
Geriatric Assessment and Management in Cancer. S. Rostoft et al
Hematologic Malignancies in Older Adults A.E. Rosko et al
Immunotherapy in Older Adults. C.J. Presley et al
Targeted Therapies in Older Adults With Solid Tumors. N.M.L. Battisti et al
Cognition in Older Adults With Cancer A. Magnuson et al
Health Equity for Older Adults With Cancer R.D. Tucker-Seeley et al
ASCO
KNOWLEDGE CONQUERS CANCER

Current Status Quo

- Cardinal Health Oncology Provider Extended Network survey of 349 providers (74% community practice) showed that 60% of oncologist did not use a formal geriatric assessment to inform on treatment decision

- Oncologist < 10 years in practice 53% reported using a GA. 15% for all versus 38% for some of their patients

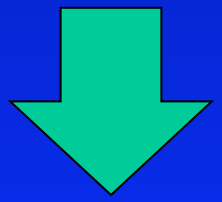
- Oncologists > 10 years in practice 37% reported using a GA, 12% in all versus 25% for some of their patients

Current Status Quo

- Most common tools to aid in treatment decision were ECOG performance status and comorbidities
- 63% recognized the Minimal Mental Exam (MMSE), 37% CGA and 37% the Cancer Aging Research Group (CARG) tool for assessments
- 19% were unaware of any geriatric assessment tools, 33% had not used any outside of a clinical trials setting

Current Status Quo

- “to cumbersome to in cooperate into routine practice”
- No added value beyond the comprehensive history and PE



Increasing education of the benefits of geriatric assessment-directed therapy could help increase the utilization

Models of Care in Geriatric Oncology

- Screen and refer model
- Shared care model
- Multidisciplinary consultative model
- Geriatric Oncologist driven
- Self administered

Models of care in Geriatric Oncology JCO 2021, Volume 39, Issue 19, 2195-2204

Models of Care in Geriatric Oncology

- CARG National Institute of Health/National Institute of Aging (NIH/NIA) R21/R33 Clinical Implementation Core CIC grant
- CIC funds infrastructure in seven cores: leadership, aging measures, analytics, clinical implementation, communication, health services, and supportive care
- ACCC created resources for community providers to support the implementation of geriatric screening and assessment – including curating a resource library of > 100 tools with a variety of options in each key domain of GA

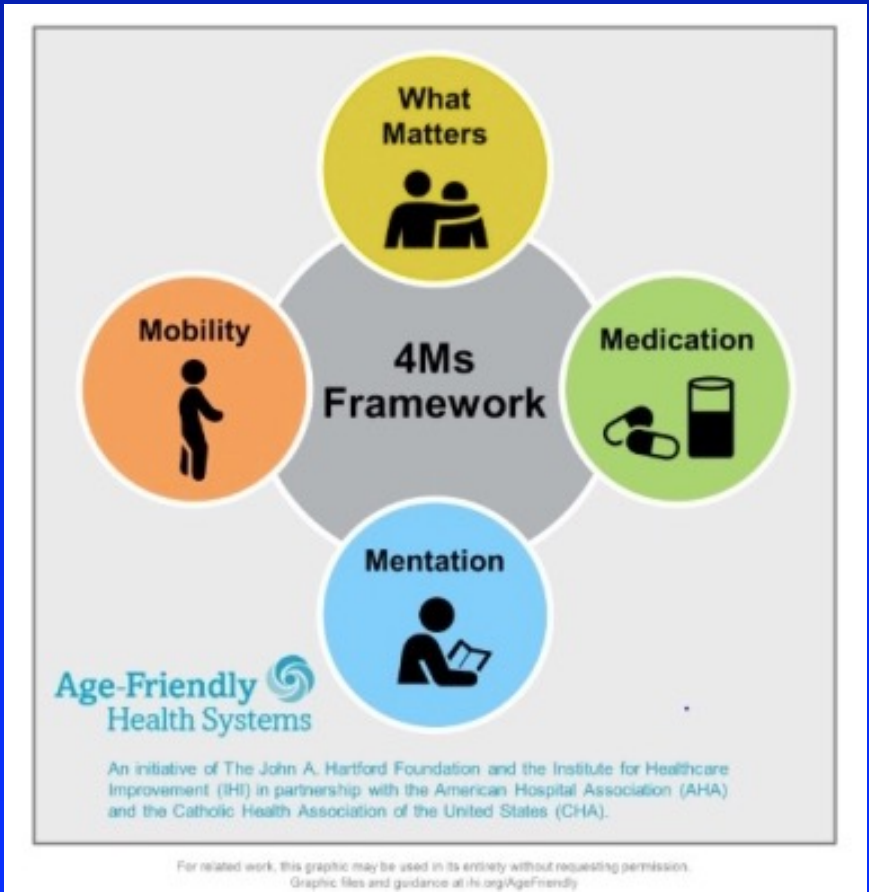
Models of care in Geriatric Oncology JCO 2021, Volume 39, Issue 19, 2195-2204

Initiatives and Care Standards

- American College of Surgeons (ACS) Geriatric Surgery Verification program (GSV) Program provides a framework to take interdisciplinary approach to continuously optimize surgical care. Includes 30 standards to improve surgical care for older adults

- ACS National Surgical Quality Improvement Program Surgical Risk Calculator includes both geriatric-specific predictors and geriatric-specific outcomes and help facilitate informed discussions regarding risk of surgery

IHI


What Matters
Mobility
4Ms Framework
Medication
Mentation
Age-Friendly Health Systems
An initiative of The John A. Hartford Foundation and the Institute for Healthcare Improvement (IHI) in partnership with the American Hospital Association (AHA) and the Catholic Health Association of the United States (CHA).
For related work, this graphic may be used in its entirety without requesting permission.
Graphic files and guidance at ihi.org/AgeFriendly

Sarcopenia

- Greek *sarx* for flesh and *penia* for loss- 1989 phrased
- Two standard deviations below the mean muscle mass of healthy younger adults using dual X-ray absorptiometry
- Decrease in anabolic hormones, particularly testosterone
- Structurally Type II fiber atrophy, loss of motor neurons, muscle denervation, neuromuscular junction instability
- Aging results in mitochondrial dysfunction by reduced mitochondrial DNA and ATP production in skeletal muscle and accumulation of reactive oxygen species

Sarcopenia

- 4th decade of life, linear decrease in muscle mass and strength while body fat increases
- Increasing interest in Oncology because of high prevalence associated with adverse outcomes
- 2007 Prado et al. showed body composition as an independent determinant of 5FU chemotherapy toxicity
- 2021 PubMed search resulted in 1821 hits

Sarcopenia in the Older Adult With Cancer, Williams et al JCO 2021,Volume 39, Issue 19 2068-2078

Sarcopenia

- Oncologic view is more focused on mortality and complications from cancer treatment, geriatric in the light of development of disability
- Cancer treatment increases the risk of sarcopenia and exacerbates pre-existing muscle wasting
- Many cancer treatments cause direct or indirect damage to the muscle tissue by pathways that up-regulate proteasome activity

Sarcopenia in the Older Adult With Cancer, Williams et al JCO 2021,Volume 39, Issue 19 2068-2078

Sarcopenia and Oncology Outcomes

- Umbrella review that included 30 meta-analysis was associated with significant poorer prognosis
- Strongly associated with postoperative complications, infections, readmission rates and length of hospitalizations
- Explaining the adverse outcomes is complex – body composition changes results in change of pharmacokinetics of both hydrophilic drugs and hydrophobic drugs
- Marker of increase cancer-related inflammatory response

Sarcopenia in the Older Adult With Cancer, Williams et al JCO 2021,Volume 39, Issue 19 2068-2078

Interventions

Number of interventions are being investigated and include:

- Physical exercise – resistance training
- Nutritional supplementation
- Hormone replacement
- Therapeutic agents promoting muscle mass

Sarcopenia in the Older Adult With Cancer, Williams et al JCO 2021,Volume 39, Issue 19 2068-2078

Immunotherapy in Older Adults with Cancer

- Changes in the microenvironment of lymphoid organs such as bone marrow and thymus
- Shifts in the relative abundance of immune cell subsets
- Alteration in the make up of circulating cytokines which control immune hemostasis
- Although cellular and immunosenescense often go hand-in - hand, emerging data suggest that these are separate consequences of physiologic aging

Immunotherapy in Older Adults in Cancer, JCO 2021 Volume 39 (19): 2115-2127

Immunotherapy In Older Adults with Cancer

- Real world ICI data found comparable efficacy
- irAE's seem to occur in similar incidence and severity as younger adults
- NCT04533451/Alliance trial ongoing to help improve understanding of IO in elderly

Immunotherapy in Older Adults in Cancer, JCO 2021 Volume 39 (19): 2115-2127

Summary

- Aging is heterogenous and age-related body changes require special attention
- Validated Assessment Screening Tools are available and interventions recommended
- Oncology and their health care system are creating geriatric frameworks to foster care towards older adults
- Sarcopenia is a marker of adverse outcomes
- Continued research is needed to improve outcomes