

Aging and Cancer

Arash Naeim, MD PHD
Director, Geriatric-Oncology Program

*“If you’re not a pediatric oncologist,
you’re a geriatric oncologist.”*

Saying in Oncology, source unknown

A 75 year old woman



Would you send her for a screening mammogram?

If she had triple negative lymph node + breast cancer would you send to a medical oncologist for adjuvant chemotherapy post-operatively ?

A 75 year old woman



In a wheelchair

Would you send her for a screening mammogram?

If she had triple negative lymph node + breast cancer would you send to a medical oncologist for adjuvant chemotherapy post-operatively ?

A 75 year old woman



In a wheelchair

Just to and from clinic

All the time

Would you send her for a screening mammogram?

A 75 year old woman



In a wheelchair

Fatigue and weakness

Arthritis

Would you send her for a screening mammogram?

A 75 year old woman



In a wheelchair due to arthritis
with a myocardial infarction last yr

Would you send her for a
screening mammogram?

A 75 year old woman



In a wheelchair due to arthritis
with a myocardial infarction last yr
Diabetes
Stroke
Moderate Chronic Renal Insufficiency
Hypertension

Would you send her for a
screening mammogram?

A 75 year old woman



In a wheelchair due to arthritis
with a myocardial infarction last yr
with diabetes, HTN, and mod CRI
with Alzheimer's dementia

Would you send her for a
screening mammogram?

A 75 year old woman



In a wheelchair due to arthritis
with a myocardial infarction last yr
with diabetes, HTN, and mod CRI
with Alzheimer's dementia
Mild to Moderate
Severe

Would you send her for a
screening mammogram?

A 75 year old woman



In a wheelchair due to arthritis
with a myocardial infarction last yr
with diabetes, HTN, and mod CRI
with mild Alzheimer's dementia
with a strong preference

Would you send her for a
screening mammogram?

If she had triple negative lymph node
+ breast cancer would you send to a
medical oncologist for adjuvant
chemotherapy post-operatively ?

Impact of Cognitive Impairment on Screening Mammography Use in Older US Women

| Kala M. Mehta, DSc, MPH, Kathy Z. Fung, MS, Christine E. Kistler, MD, Anna Chang, MD, and Louise C. Walter, MD

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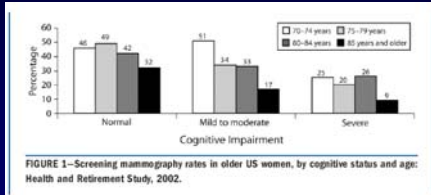


FIGURE 1—Screening mammography rates in older US women, by cognitive status and age: Health and Retirement Study, 2002.



ATHENA Breast Network
 UCSF, UCLA, UCSD,
 UCI, UCD + UCB
 PI: Esserman, Laura
 UCLA Site PI: Naeim, Arash

Goal

Follow a cohort of 120,000 women who present for a screening mammogram

Screening in the Older Individuals

Using the Vulnerable Elders Survey (VES-13) and Comorbidity to Assess Life Expectancy

The Basics

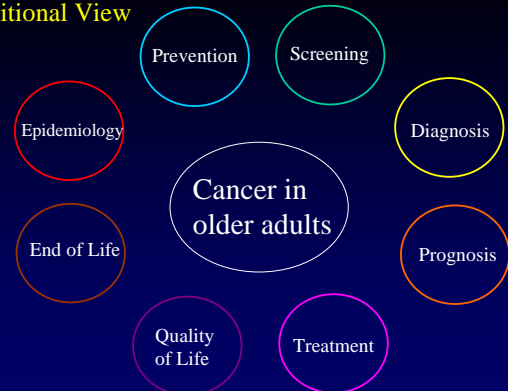
What age represent aging?

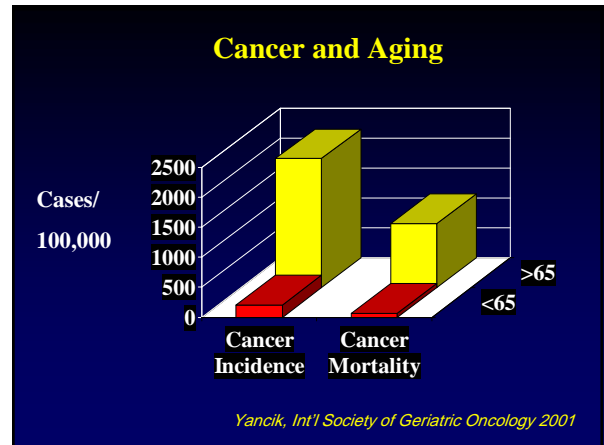
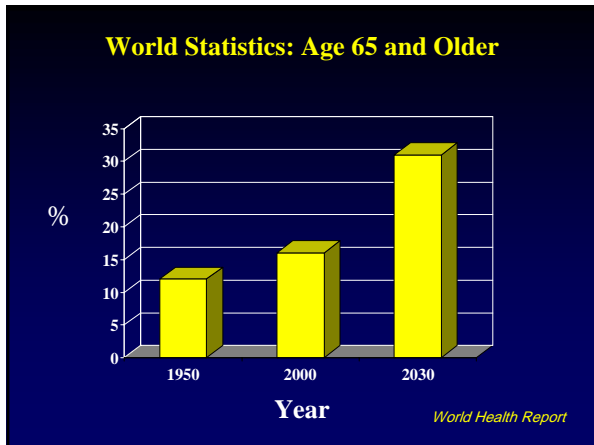
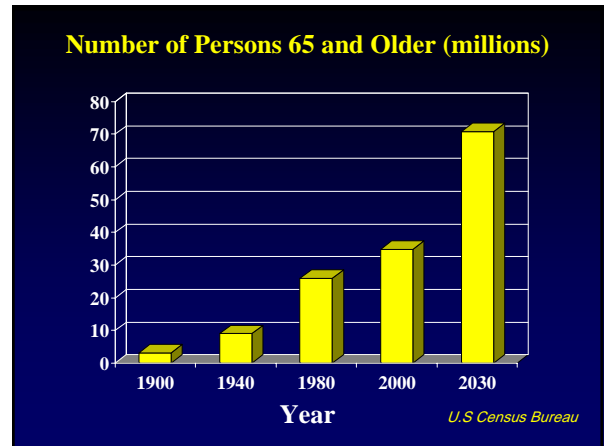
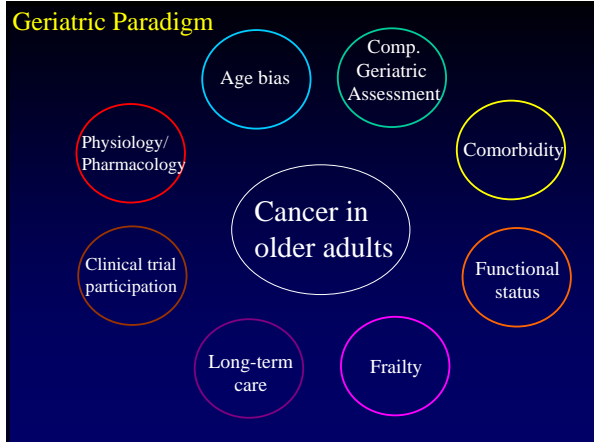


What is geriatric oncology?

- No one precise definition of a 'geriatric' patient; commonly 65 or 70 used
- Among geriatricians/gerontologists, 65-74 are 'young old', 75-84 are 'medium old', and 85+ are 'oldest old'
- Overall it is clear that aging has led to an increased focus on cancer in older adults

Traditional View





The Population is Aging
 The Number of Older Adults With Cancer is on the Rise

↓

Are we prepared?

- ### The Questions We Face in Daily Practice are Not Addressed in Clinical Trials
- Who will die of disease vs. with disease?
 - Who is vulnerable to cancer therapy toxicity?
 - How should I adjust the therapy based on:
 - their functional status
 - their comorbid illnesses
 - their social situation
- Who is Frail?**

Do We Address the Questions that Patients Want to Know?

Doctor, if I take the therapy...

- will I be hospitalized?
- will I be functionally impaired?
- will I be cognitively impaired?
- what does my family need to prepare for?
- what is the quality of my survival?

Will I become frail?

Projected life expectancy (years)

Age now	Life Expectancy	Age of Death
65	17.7	82.7
70	14.3	84.3
75	11.2	86.2
80	8.5	88.5
85	6.3	91.3
90	4.5	94.5
95	3.3	98.3
100	2.5	102.5

National Vital Statistics Report

Comorbidity

Comorbidity

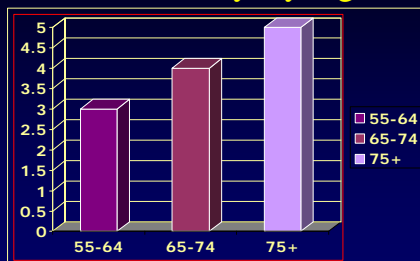
Definition:

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

Key questions:

1. Is the patient going to die from cancer or another medical problem?
2. Will another medical problem limit the ability to tolerate treatment?

Comorbidity By Age



Yancik R. Cancer 1998; 82:2123-2134

Age, comorbidity & life expectancy

- Synergistic interaction between age & comorbidity (e.g. as measured by Index of Co-Existent Disease, ICED)

Age	ICED 0	ICED 1	ICED 2	ICED 3
65	12.5 y	10.7 y	7.1 y	2.3 y
70	9.8 y	8.3 y	5.4 y	1.6 y
75	7.5 y	6.3 y	3.9 y	1.1 y

Albertsen JAMA 1995; 274:626

Major comorbid conditions in older cancer patients

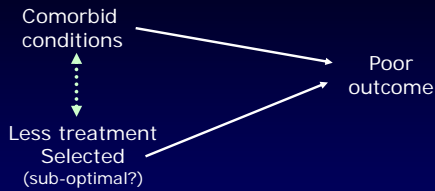
Condition	Percent
Hypertension	42.9
Heart disease	39.1
Arthritis	34.9
Gastrointestinal problems	31.0
Anemia	22.6
Eye Problems	19.0
Urinary Tract	18.0
Previous cancer	15.4
Gallbladder problem	14.9
COPD	14.5
Diabetes	12.8

Yancik Cancer 1997; 80:1273

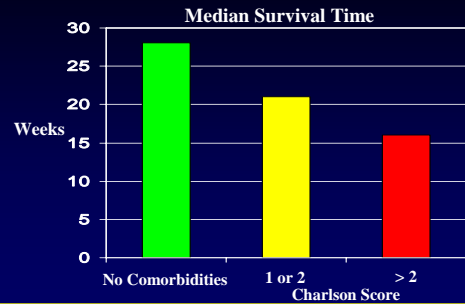
Impact of comorbidity

- ↑ risk of short-term mortality and complications after surgery/radiation
- ↑ risk of complications after chemotherapy
- ↓ overall survival
- ↑ likelihood of dying from other causes

Bias



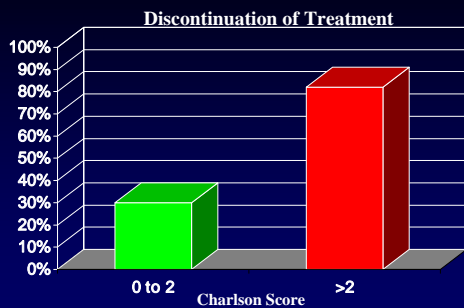
Comorbidity → Decreased Survival in Patients with Lung Cancer



Higher comorbidity score → worse survival

Frasci et al. J Clin Oncol, 2006

Increased Comorbidity Correlates with Cancer Treatment Discontinuation



Higher comorbidity score → more likely to discontinue treatment

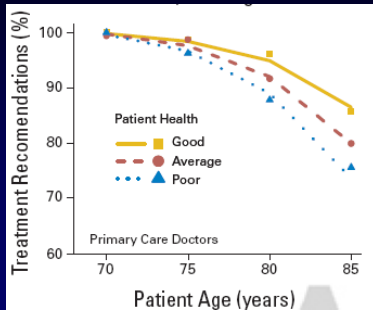
Frasci et al. J Clin Oncol, 2006

Adjuvant Therapy

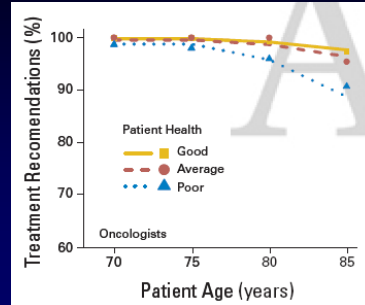
	AR (Cancer)	AR (Comorbidity)	AR Reduction with Chemotherapy
HEALTHY			
Breast (ER+)*	2.8%	19.9%	0.3%
Breast (ER-)#	57.3%	11.3%	4.8%
Colon (Stage III)^	31.5%	4.9%	13.4%
Lung (Stage IIB)-	32.4%	3.6%	8.5%
VULNERABLE			
Breast (ER+)*	0.6%	96.4%	0.0%
Breast (ER-)#	23.1%	76.1%	0.2%
Colon (Stage III)^	19.9%	68.4%	3.3%
Lung (Stage IIB)-	41.1%	54.9%	1.6%

AR= Absolute Risk of Death for Breast (10 years), Colon (5 Years), Lung (5 Years) Models
 * Estrogen Receptor (+), Grade 1 tumor, 1.1 cm, No nodal involvement
 # Estrogen Receptor (-), Grade 3 tumor, 2.0 cm, 4-9 nodes involved
 ^ T3, 1-3 Nodes
 - T2, N1
 VULNERABLE = 2 major comorbid conditions

To Treat or Not: PCPs



To Treat or Not: Oncologists



ATHENA Breast Network
UCSF, UCLA, UCSD,
UCI, UCD + UCB
PI: Esserman, Laura
UCLA Site PI: Naeim, Arash

Goal

Follow a cohort of 5,000 women diagnosed with breast cancer

Appropriateness of Adjuvant Therapy in Older Women with High Comorbidity Burden

Identify women for whom adjuvant treatment may not be beneficial



Medscape © <http://www.medscape.com>

Frailty

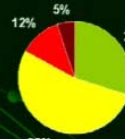
The Oncologist's Perspective of Frailty

ECOG Performance Status

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

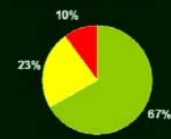
Evaluation: Is ECOG PS enough?

Oncology patients aged ≥ 70 yo



Extermann et al., JCO 1998

Patients age ≥ 70 yo undergoing chemotherapy:



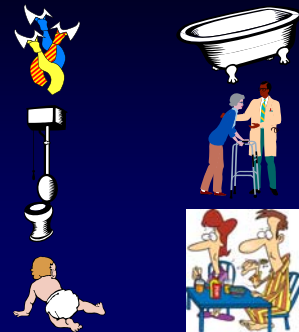
Chen et al., Cancer 2003

The Geriatrician's Perspective of Frailty

Geriatrician's Assessment of Function Activities of Daily Living (ADLs)

Basic self-care skills

- Dressing
- Bathing
- Toileting
- Transfer
- Continence
- Eating



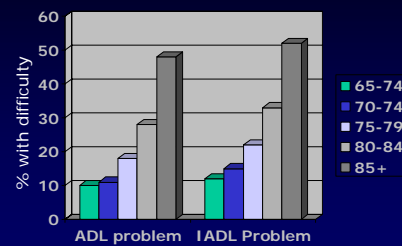
Geriatrician's Assessment of Function Instrumental Activities of Daily Living

Higher order function

- Shopping
- Housekeeping
- Transportation
- Laundry
- Telephone
- Finances
- Medications



Difficulty with ADLs and IADLs by Age



How do we apply geriatric principles to older adults with cancer?

Assistance with IADLs → Worse Survival in Patients with Lung Cancer

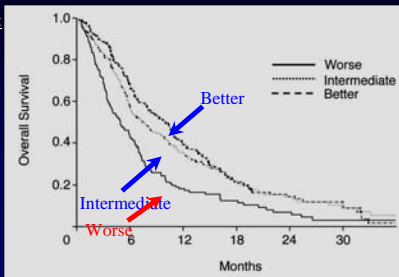
- Multicenter Italian Lung Cancer in the Elderly Study
- Advanced non-small cell lung cancer (Stage IV or IIIb)
- 566 patients
- Age 70 and older
- Association between IADL assistance and survival

Maione et al. *J Clin Oncol*. 2005

Assistance with IADLs → Worse Survival in Patients with Lung Cancer

Categories of IADLs:

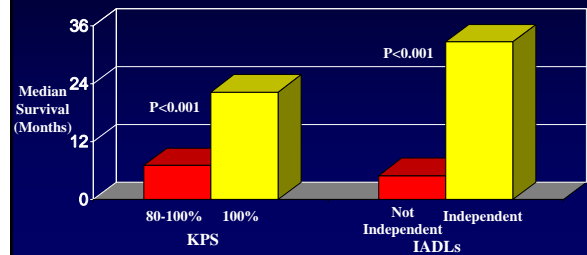
- Better: Score of 100%
- Intermediate: Score of 51-99%
- Worse: Score of 0-50%



Maione et al. *J Clin Oncol*. 2005

Decreased Functional Status → Poorer Survival in Patients with AML

- 63 patients with newly diagnosed AML



Wedding et al. *J Cancer Res Clin Oncol*. 2006

What about the “fit” older adults?



Will chemotherapy make them frail?

UNDERSTANDING THE TREATMENT PREFERENCES OF SERIOUSLY ILL PATIENTS

Special Article

UNDERSTANDING THE TREATMENT PREFERENCES OF SERIOUSLY ILL PATIENTS

TERI R. FRIED, M.D., ELIZABETH H. BRADLEY, Ph.D., VIRGINIA R. TOWLE, M.Phil., AND HEATHER ALLORE, Ph.D.

I would rather die than take a treatment that causes:

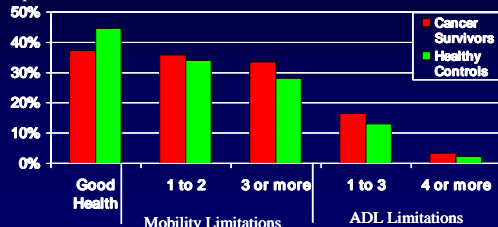
- functional impairment: 74%
- cognitive impairment: 88%

Fried et al. *NEJM* 2002; 346 (14): 1061

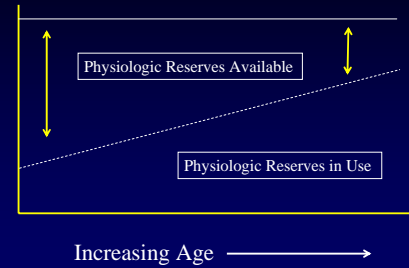
Older Cancer Survivors Need More Assistance with ADLs

Older Cancer Survivors...

- Were less likely to report excellent or good health (P<0.001)
- Reported more mobility limitations (P<0.001)
- Reported more limitations with ADLs (P=0.01)



Which “Fit” Individual will Become “Frail?”



Understanding Frailty in Oncology Practice: The Future

- Understanding frailty is critical to geriatrics & oncology
- Cancer: a perfect model for understanding frailty
- Definition of frailty in older adults with cancer:
 - Combination of clinical and biological factors
- Guides therapeutic decision making
- Identify signs of vulnerability
- Common language: “functional age”



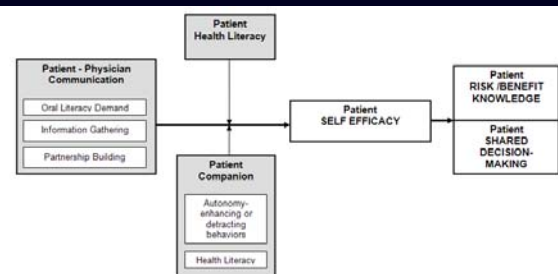
Goal: Maintain function and independence

Communication and Shared Decision-Making with Older Cancer Patients

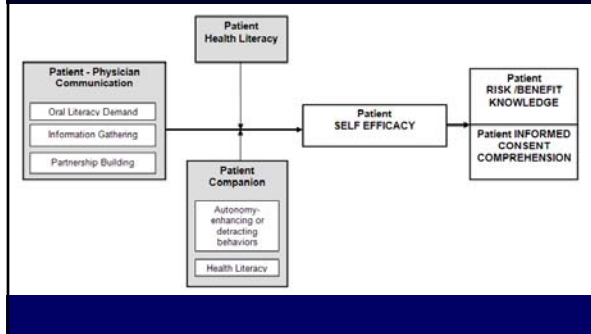
Its Complicated

- **Health Literacy** is defined as “the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions”.
- **Oral Literacy Demand** is defined as the use of technical terms, general language complexity, and structural aspects of dialogue such as pacing, density, and interactivity.

Conceptual Model



California Breast Cancer Research Program Idea Grant

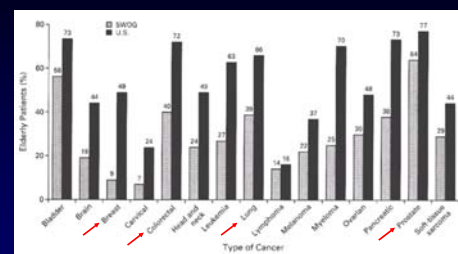


Is our approach to older cancer patient's evidence-based?

Limited oncology evidence base

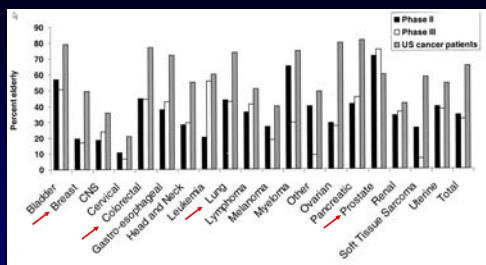
- Poor recruitment of older adults into clinical trials
- Limited # of older adults even in many large trials to facilitate subgroup analyses
- Highly selected older adults in clinical trials (limited comorbidity, not disabled/frail, cognitively intact)

SWOG Trials



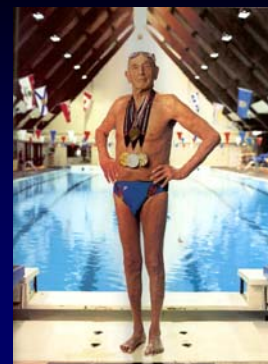
Hutchins LF et al, 1999

ECOG Trials



Lewis JH et al, 2003

Who is placed on Clinical Trials?



Clinical Trials in the Elderly

Barriers

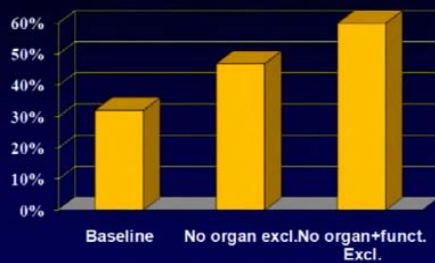
CALGB 9670: Barriers to Trials

Variable	< 65 years	65+ years
	Median 50	Median 77
Offered Trial *	51%	35%
Offered and Accepted	56%	50%

In multivariate analysis **AGE was only independent risk factor** for offering trial. Race, co-morbidity, stage, education, marital status, satisfaction with care NOT predictive.

Kemeny et al, J Clin Oncol

Removing barriers



Lewis et al, JCO 2003

Clinical Trial Design Issues

- Age versus Frailty
- Dedicated Trial versus Subgroup Analysis
- Interest from Pharmaceutical Companies
- Outcomes (Traditional versus Novel)

GI-04 : Phase II frontline oral chemo + IV targeted agent in frail and elderly patients with metastatic colorectal cancer

Measure	Outcome (n=40)
Response	
Best response, no. (%)	
CR	2 (5)
PR	14 (35)
SD	16 (40)
PD	8 (20)
Response rate (CR + PR), % (95% CI)	40 (24.8-55.2)
Clinical benefit rate (CR + PR + SD), % (95% CI)	80 (67.6-92.4)
TTP	
Median TTP, months (95% CI)	7.2 (4.4-12.1)
6-month TTP rate ± SE, %	56.2 ± 8.3
12-month TTP rate ± SE, %	32.8 ± 8.9

CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; SE, standard error; TTP, time to progression.

Geriatric-Hematology



Other Areas of Research

- Symptom Clusters and Management
- Clinical Trials of Supportive Agents
- Comparative Effectiveness Research

Increasing Recognition

- Hartford Foundation
- Sub-Specialty Societies (ASCO, ASH, AGS, ASP)
- NIH (NCI and NIA) – P20, U01, R01