Will you still screen me, will you still treat me, when I'm 64? What about 84?

(A brief tour of the wonderful world of geriatric oncology)

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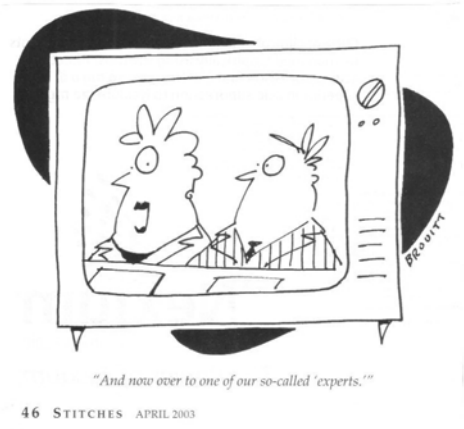
Learning objectives

- To describe the burden of cancer in older adults
- To describe special considerations of cancer in older adults
- To briefly review emerging research themes in the area of geriatric oncology



"If you're not a paediatric oncologist, you're a geriatric oncologist."

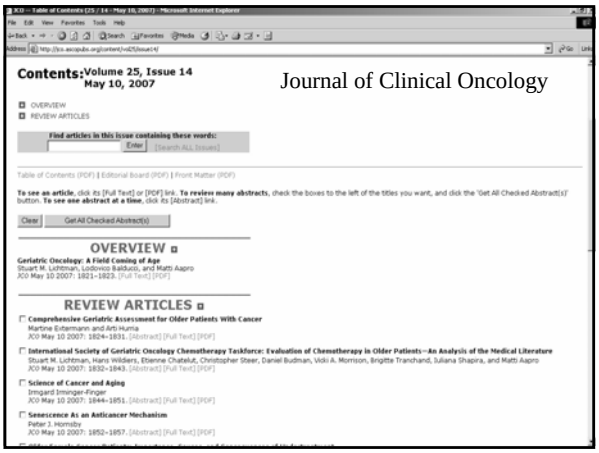
Saying in Oncology, source unknown

Outline

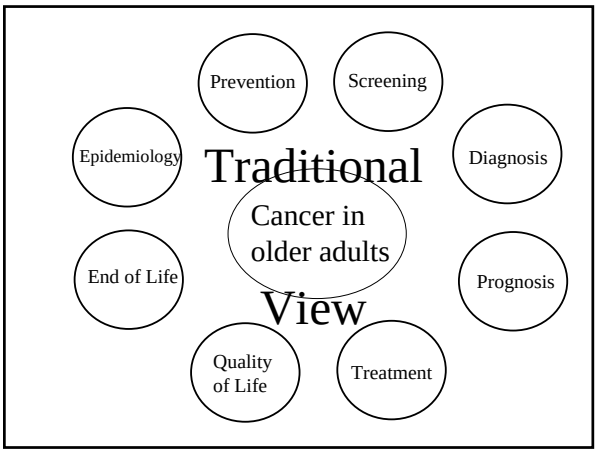
- What is geriatric oncology?
- Burden of cancer in older adults
- What's so special about growing old?
- Emerging research in geriatric oncology
- Summary

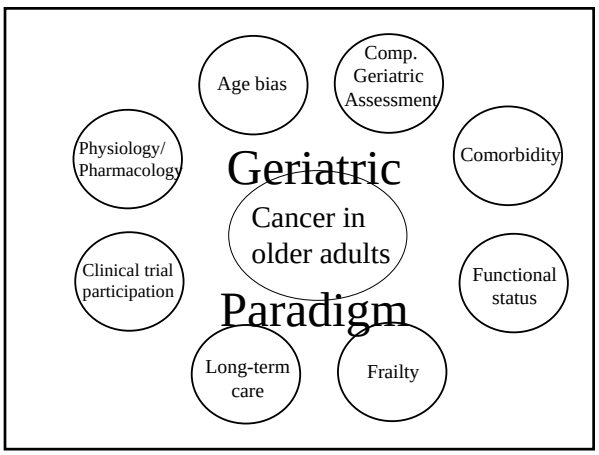
What is geriatric oncology?

- 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



Journal of Clinical Oncology

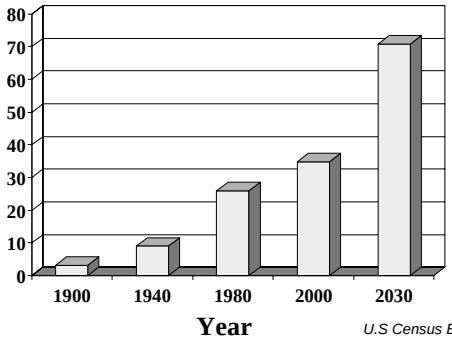




Outline

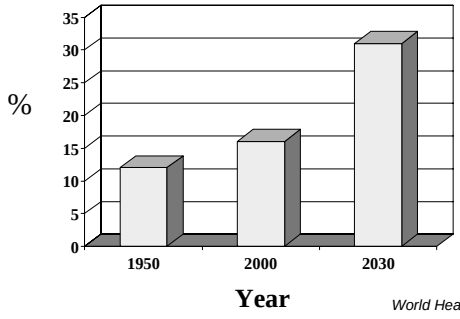
- What is geriatric oncology?
- Burden of cancer in older adults

Number of Persons 65 and Older (millions)



U.S Census Bureau

World Statistics: Age 65 and Older



World Health Report

The Population is Aging

Age ≥ 65: Fastest growing segment in Canada

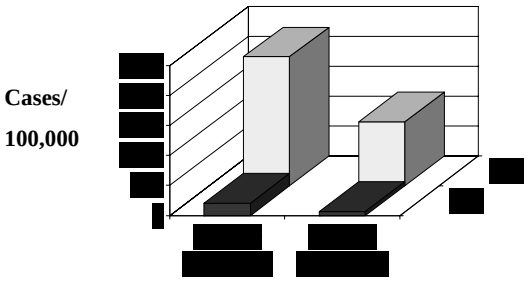
By 2030:

Age 65 and older: double

Age 75 and older: triple

Age 85 and older: double

Cancer and Aging

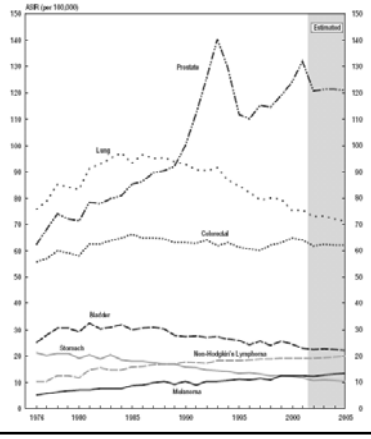


Yancik, Int'l Society of Geriatric Oncology 2001

Burden of cancer in older adults

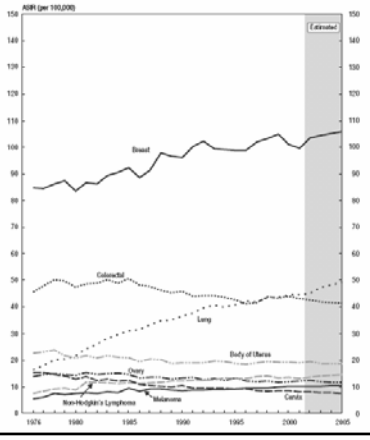
- Older adults are fastest growing age group in Western countries
- About 60% of all cancers occur in age 65+
- 71% of all cancer deaths in age 65+
- Odds of dying from cancer are 16-fold higher in people age 65+ compared to <65

2005 Cancer Incidence Data: Men



From Canadian Cancer Society Cancer Statistics 2005

2005 Cancer Incidence Data: Women



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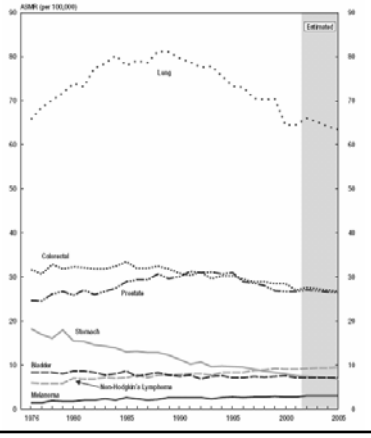

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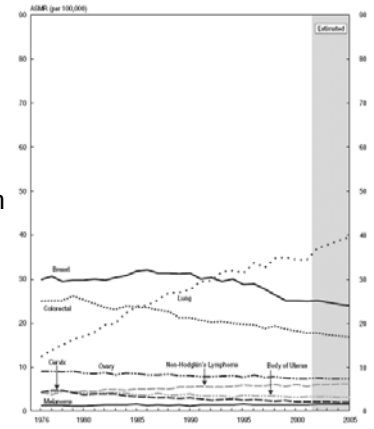

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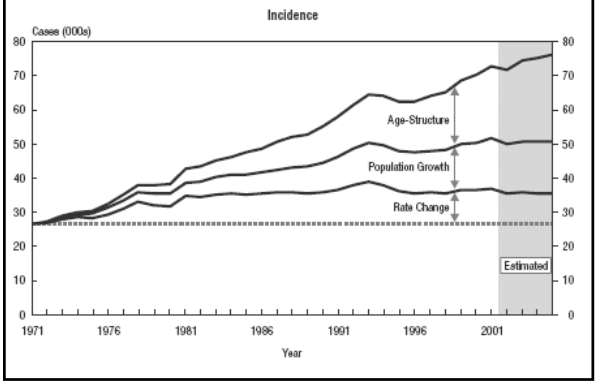
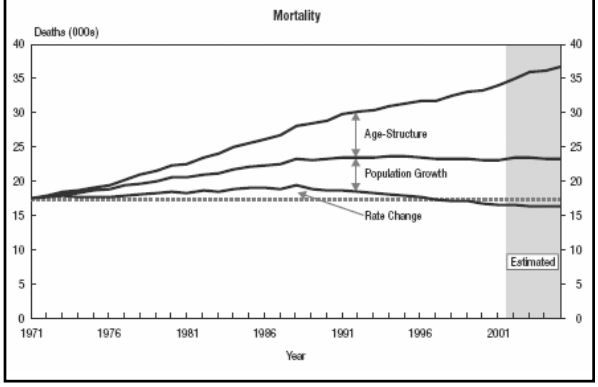
Factors accounting for increased cancer incidence



Factors accounting for increased cancer mortality



Outline

- What is geriatric oncology?
- Burden of cancer in older adults
- What's so special about growing old?

"I'm getting old, Jim. Today, instead of jumping, I had to stretch gently to a conclusion."

What's so special about growing old?

- Decreasing life expectancy
- Increasing comorbidity (competing causes of mortality)
- Increasing cognitive and functional impairment
- Increasing frailty
- Altered pharmacokinetics/dynamics as well as *homeostenosis*
- Limited oncology evidence base

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

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?

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

30-day mortality after radical prostatectomy

Age	Mortality	Any complication
<50	0%	20.4%
50-59	0.21%	17.2%
60-69	0.58%	20.6%
70-79	0.66%	26.9%

- unadjusted rates

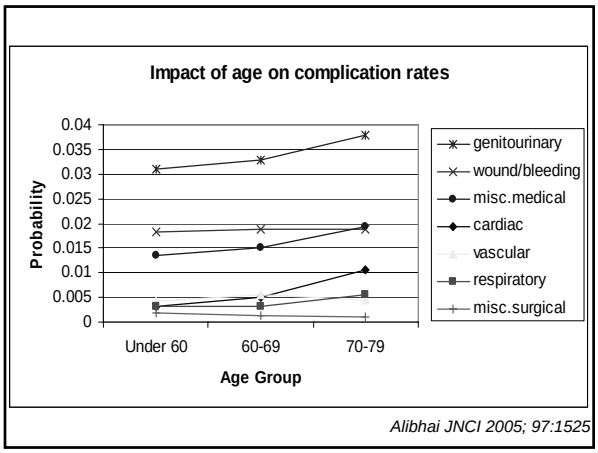
Alibhai JNCI 2005; 97:1525

Predictors of 30-day mortality

Variable	Multivariable
Age (per decade)	2.04 (1.22, 3.39)
Year of Surgery	0.58 (0.33, 1.01)
Cardiovascular disease	2.43 (1.12, 5.26)
Stroke	7.84 (1.84, 39.77)

c-statistic=0.69

Alibhai JNCI 2005; 97:1525



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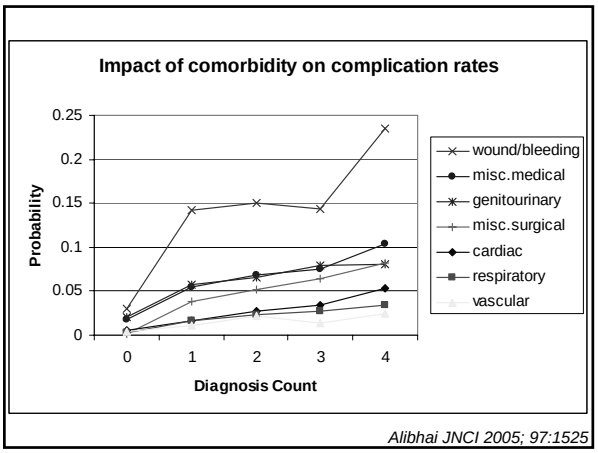

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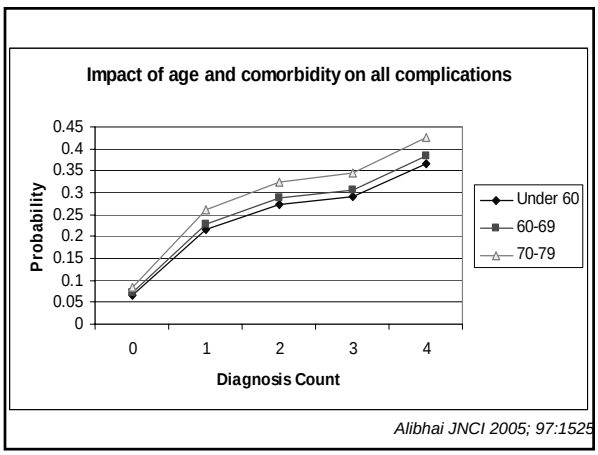

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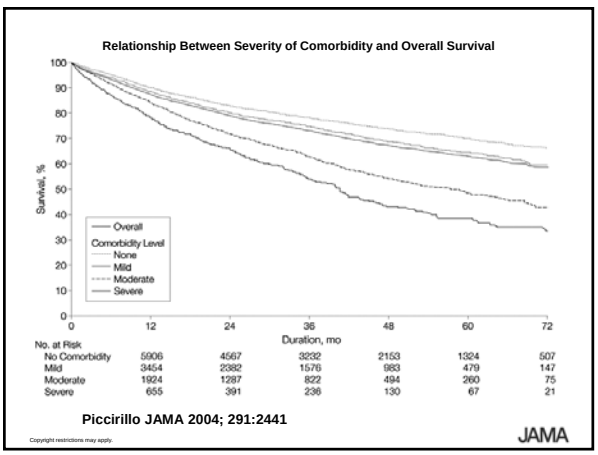
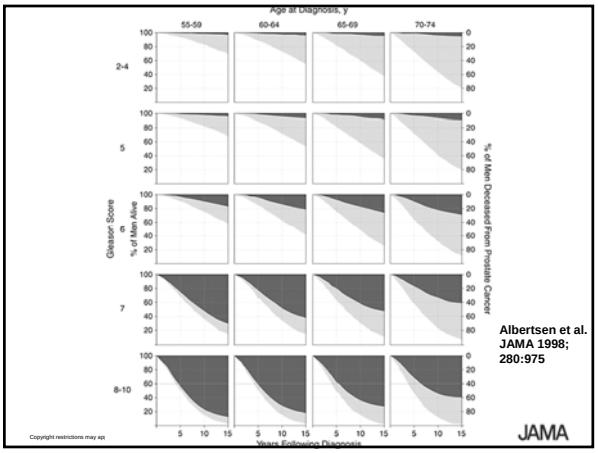


Age, comorbidity & life expectancy

• Synergistic interaction between age & comorbidity

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



Remaining life expectancy

- Key variables in determining remaining life expectancy:
  - Age
  - Comorbidity
  - Disability

Impact of disability

• Several studies have demonstrated an excess risk of morbidity and premature mortality from dependence in activities of daily living (ADLs)

• Independent of age and comorbidity

• Likely a marker of frailty

• In one high quality study, dependence in 1 or more Instrumental ADLs associated with 50% increased risk of dying over next 5 years (JAMA 1998; 285:2750)

Calculating remaining life expectancy

Scenario	Male	Female
Age 75, no comorbidity, indep. IADLs	12.33 y	15.18 y
Age 75, mild comorbidity, indep. IADLs	9.70 y	12.44 y
Age 75, moderate comorbidity, indep. IADLs	6.12 y	8.45 y
Age 75, moderate comorbidity, dependent 2+ IADLs	4.49 y	6.53 y

Altered pharmacology

• Numerous age-related changes in host organs/tissues at both pharmacokinetic and pharmacodynamic levels

• Pharmacokinetics
  – Absorption
  – Distribution
  – Metabolism
  – Elimination

• Pharmacodynamics
  – Altered tissue sensitivity

Key pharmacokinetic changes

• ↓ absorption surface
• ↑ body fat
• ↓ body water
• ↓ albumin concentration
• ↓ liver blood flow and size
• ↓ GFR (7-10 mL/min/decade after age 30)

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

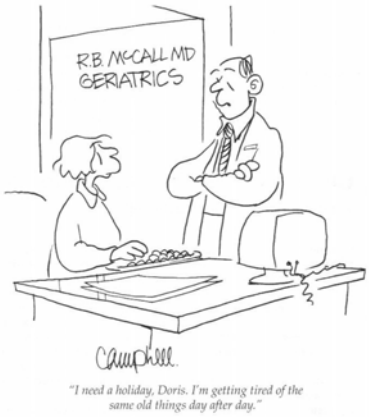
• Highly selected older adults in clinical trials (limited comorbidity, not disabled/frail, cognitively intact)

Outline

- What is geriatric oncology?
- Burden of cancer in older adults
- What's so special about growing old?
- Emerging research in geriatric oncology

Emerging research

- Age bias – next steps
- Comprehensive geriatric assessment
- Screening – when do we stop (if ever)?
- Elder-specific clinical trials



"I need a holiday, Doris. I'm getting tired of the same old things day after day."

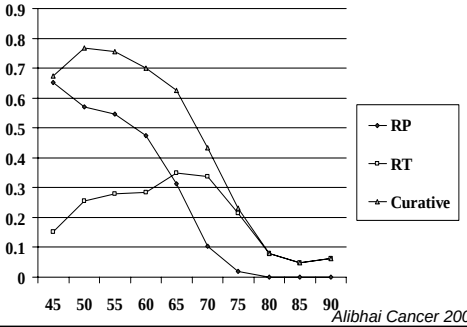
Age bias

- Systematic discrimination against people simply on the basis of age
- Often synonymous with inappropriate (under) treatment

Age bias

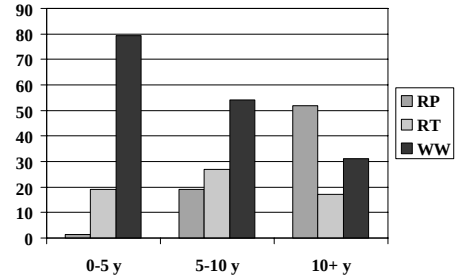
- Numerous studies in oncology have shown that older people are:
  - Less aggressively screened
  - Less systematically staged
  - Receive less standard surgical therapy
  - Receive less adjuvant radiation/chemotherapy
  - Receive less cosmetic surgical reconstruction consultation
  - Receive less dose-intense chemotherapy
  - Receive CSF's less often with chemotherapy
  - Receive strong analgesic and anti-emetic drugs less often

Observed probability of receiving treatment within 6 months by age group (n=5,192)



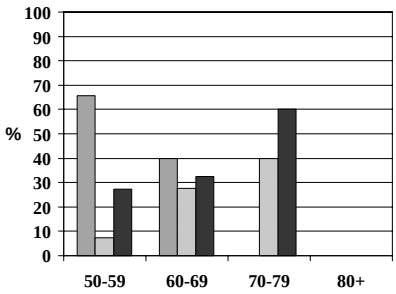
Alibhai Cancer 2004; 100:72

Receipt of treatment based on predicted life expectancy, all age groups



Alibhai Cancer 2004; 100:72

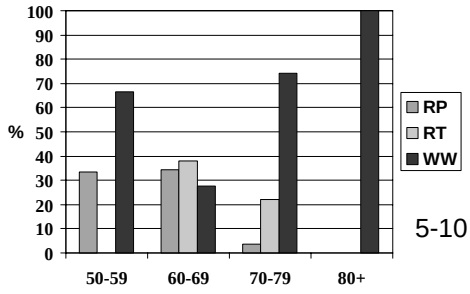
Receipt of treatment by age group, stratified by estimated remaining life expectancy



>10 years

Alibhai Cancer 2004; 100:72

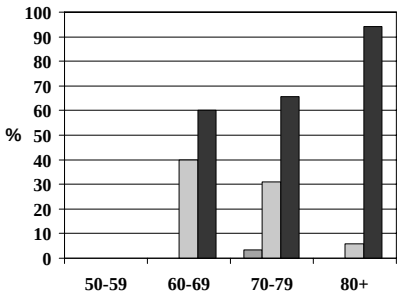
Receipt of treatment by age group, stratified by estimated remaining life expectancy



5-10 years

Alibhai Cancer 2004; 100:72

Receipt of treatment by age group, stratified by estimated remaining life expectancy



<5 years

Alibhai Cancer 2004; 100:72

Age bias

- Lots of studies documenting existence of age bias
- Emerging data on various reasons
- Limited intervention studies looking at ways to minimize age bias
  - Some limited success with geriatric oncology specialty clinics and/or CGA-based approaches

Comprehensive geriatric assessment

"A multidisciplinary diagnostic process intended to determine a frail elderly person's medical, psychosocial, and functional capabilities and limitations in order to develop an overall plan for treatment and long-term follow-up"

Rubenstein, 1982

Comprehensive geriatric assessment

- Key components of CGA:
  - Comorbidity
  - Polypharmacy
  - Functional status
  - Cognitive function
  - Mood
  - Social support
  - Nutritional status

CGA – Who needs it?

- 7 studies of geriatric oncology population:
  - Ages ranged from 68 to 79
  - 31-86% independent in basic ADL's
  - 26-52% independent in instrumental ADL's
  - 14-40% had significant depressive symptoms
  - 25-51% had cognitive impairment
  - Taking a mean of 6 medications

Extermann J Clin Oncol 2007; 25:1824

CGA – Does it work?

- Number of studies using various forms of CGA in oncology settings
- Improved detection rates of comorbidity, polypharmacy, nutritional issues, need for social support, disability, depression
- Some suggestion of decreased age bias in use of surgery and primary/adjuvant chemotherapy

CGA – Does it work?

- Limitations:
  - No randomized studies
  - Unclear if survival or disease control impacted
  - Unclear which method(s) and population(s) optimal for CGA

(P.S. Canada is way behind US and several European nations)

Cancer screening – when to stop?

- Screening asymptomatic individuals to detect early cancers which may be curable
- Use diagnostic tests with high sensitivity
- Natural history of disease can be changed by intervention
- Benefits outweigh risks
- What about elderly?
  - Diminishing benefits with increasing age
  - Increased risk of harms

Cancer screening guidelines

Malignancy	ACS	CTFPHC	USPSTF
Breast	CBE & Mammogram yearly after age 40	CBE & Mammogram every 1-2 y age 50-69	Mammogram every 1-2 y age 50-69
Cervical	Pap every 2-3 y until age 70*	Pap every 3 y until age 69*	Pap every 3 y until age 69*

ACS = American Cancer Society; CTFPHC = Canadian Task Force on Preventive Health Care; USPSTF = US Preventive Services Task Force; CBE = Clinical breast exam
* - if 3 prior Pap smears were normal

Cancer screening guidelines

Malignancy	ACS	CTFPHC	USPSTF
Colorectal	Age 50+ either FOBT yearly OR flex sig every 5 y OR colonoscopy every 10 y OR DCBE every 5 y	Age 50+ FOBT every 1-2 y +/- flex sig (interval not specified)	Age 50+ FOBT yearly +/- flex sig (interval not specified)
Prostate	Annual PSA + DRE age 50+ if LE>10 y	Not routinely recommended	Not routinely recommended

FOBT = Faecal occult blood test; DCBE = Double contrast barium enema; PSA = Prostate-specific antigen; DRE = digital rectal exam

Cancer screening – when to stop?

- Many guidelines do not include age limits to stop screening
- Primary evidence base very limited because of lack of inclusion of sufficient numbers of older adults
- If age limits exist, these are not rational (i.e. do not take into account factors such as comorbidity and disability that impact remaining life expectancy)

Cancer screening – when to stop?

- Researchers are beginning to tackle this by:
  - Constructing fancy decision-analytic models to quantify risks/benefits
  - Doing observational cohort and nested case-control studies using large population-based registries or longitudinal clinical databases

Elder-specific clinical trials

- Some geriatric oncologists have recommended/conducted elder-specific clinical trials to target recruitment of elders and answer age-relevant oncology questions (e.g. treatment of elderly lymphoma)
- Enhanced recruitment compared to traditional trials with broad age range inclusion criteria
- Somewhat more generalizable older oncology patients in trials

Elder-specific clinical trials

- Has not adversely affected recruitment to general cancer trials to date but experience limited
- BUT risks of using less toxic/less efficacious regimens in non-randomized studies
- May be most appropriate to:
  - Answer questions about safety/efficacy of established drug in specific older populations
  - Determine non-inferiority of less toxic regimens compared to standard practice

"Wind up your presentation — he's losing bone mass."

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Summary

- Cancer disproportionately affects older adults in terms of incidence, morbidity, and mortality
- Older patients with cancer have more comorbidity, disability, polypharmacy, and altered pharmacology that impact all aspects of oncology research and practice
- Age bias exists in most areas of oncology
- Evidence base to treat older adults with cancer limited in several ways

Summary

- Complex interactions between age, comorbidity, and disability with respect to short-term and long-term outcomes in older cancer patients
- Lots of emerging research ranging from minimizing age bias to setting rational limits on screening to use of CGA to optimize oncology practice
- Lots of opportunities for more work