GERIATRIC ONCOLOGY
An Introduction

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Demographics of cancer and aging

Chronological age vs. functional age

The aging process – Impact on organs and systems

Comprehensive Geriatric Assessment

Chemotherapy toxicity in older patients – Prediction scores

Older patients in clinical research

Concluding remarks
LEARNING OBJECTIVES

At the end of this module you are expected to:

Understand the relationship between cancer and aging

Understand the particular issues, including frailty, that affect cancer management among older patients

Understand how comprehensive geriatric assessment works and what its uses are in oncology – including in predicting chemotherapy toxicity

Understand the challenges for including older patients in clinical trials
Europe has a large older population...That will get even larger!

**Table 1: Population and Demographic Indicators**

<table>
<thead>
<tr>
<th></th>
<th>Europe^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (in millions)</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>591</td>
</tr>
<tr>
<td>2050*</td>
<td>542</td>
</tr>
<tr>
<td>Population change 2007 to 2050, %</td>
<td></td>
</tr>
<tr>
<td></td>
<td>–8.3</td>
</tr>
<tr>
<td>Average age</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>38.9</td>
</tr>
<tr>
<td>2050*</td>
<td>47.3</td>
</tr>
<tr>
<td>Fertility rate</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>1.50</td>
</tr>
<tr>
<td>Under 15 year olds, %</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>16</td>
</tr>
<tr>
<td>2050*</td>
<td>15</td>
</tr>
<tr>
<td>Over 65 year olds, %</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>16</td>
</tr>
<tr>
<td>2050*</td>
<td>28</td>
</tr>
<tr>
<td>Life expectancy</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>76.0</td>
</tr>
<tr>
<td>2050*</td>
<td>82.0</td>
</tr>
</tbody>
</table>

^1 Figure 2 – EU28 population by age and sex (2013 and 2000)

^2 Projection

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Demographics of cancer and aging

Most adult cancer types increase in incidence with age

In developed countries people with 75+ years represent around 1/3 of cancer patients

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Demographics of cancer and aging

Cancer is more common among older patients for multiple reasons:

- The accumulation of mutations along an extended lifespan
- Reduced fitness of intracellular mechanisms that protect from cancer
- A pro-tumourigenic tissue environment
- Immunosuppression
GERIATRIC ONCOLOGY
Demographics of cancer and aging

Why is cancer more common among older people?

Reprinted from The Cell, 153(6), Lopez-Otin C, et al. The Hallmarks of Aging, 1194-217, Copyright 2013, with permission from Elsevier.
What does being older mean?

- Older is a subjective cultural concept that varies from culture to culture depending on a mixture of health-related, social and economic factors.
- In industrialised societies, 70 years old is a standard cut-off point used to define a person as older; however, in other, poorer or more traditional societies, a lower age may be more appropriate (such as 65, 60, or even 55).
- Persons with the same chronological age can have widely different functional ages.

In geriatric oncology, it is functional age that determines management – and, therefore, a great deal of effort is dedicated to accurately evaluating functionality and maintaining it during treatment.
Aging is a heterogeneous process

Not all “young persons” are healthy and functional

Not all “older persons” are sick and dependent

ADLs, activities of daily living; IADLs, instrumental activities of daily living.

The aging process – Impact on organs and systems

Aging leads to decline in organ function – including kidney function, heart, respiratory and nervous system, along others.

This decline can be less than obvious based on tests alone, as under normal circumstances, function may be adequate for necessity.

During physiologically stressful moments (such as surgery, chemotherapy, radiotherapy), functional reserve is necessary and thus limitation may be revealed.
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The aging process – Impact on organs and systems

**Heart:** Decreased heart rate, decreased responsiveness to adrenergic stimuli, increased afterload

**Brain:** Neuronal loss, changes in synaptic function, hyperactivation of microglial cells

**Immune system:** Reduced immune response to aggressors

**Lungs:** Decreasing lung volumes and maximal rates of airflow; decreasing forced vital capacity; decreased diffusing capacity

**Kidney:** Including renal cortical loss; progressive decrease in glomerular filtration rate and renal blood flow

The end result = increased risk of acute illness and of complications during cancer treatment
Frailty is a state of increased vulnerability to stress, which increases the risk of adverse outcomes – during cancer treatment.

It is very important to note that risk factors for frailty include psychological and social issues, such as being in a minority ethnic group, being unmarried or being depressed.
Geriatric Oncology

The aging process – Frailty

Frailty impacts on surgical outcomes – 432,828 patients

Can frailty be reversed or its onset delayed?

Some data suggests that group-based intervention with exercise can be useful\(^1\)

Guidelines suggest\(^2\):

- Physical activity programmes or nutritional interventions or a combination of both
- Interventions based on tailored care and/or geriatric evaluation and management
- Interventions based on cognitive training (alone or in combination with exercise and nutritional supplementation)

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The aging process – Frailty – Perioperative interventions

Patients aged ≥65 years
GI tumours
Programmed surgery
N=160

CGA + Perioperative Geriatric Intervention

Standard of Care

- Significantly shorter post-op LOS (5.9 vs. 8.2 days; P=0.02)
- Lower rates of post-op ICU use (13.3% vs. 32.4%; P<0.05)
- Readmission rates were not significantly different (16.7% vs. 25.0%; P=0.36)

CGA, Comprehensive Geriatric Assessment; LOS, length of stay.
Higher risk of disability, delayed convalescence and permanent loss of functionality

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The aging process – Functionality and stress

Higher risk of disability, delayed convalescence and permanent loss of functionality
GERIATRIC ONCOLOGY IN PRACTICE

First visit to discuss treatment:
- Patient history
- Cancer
- G8 screening tool
- Life expectancy

G8 ≤14
- Full CGA
  - Identification of domains
  - Proposed geriatric interventions

Decision making
- Evaluate patient autonomy or need for surrogate decision making
- Prognosis vs. life expectancy
- Benefit vs. toxicity of treatment
- Discuss patient’s priorities and goals
- Possible social and economic issues that may affect

No need of full CGA

G8 >14

No treatment

Treatment

Follow-up during treatment
GERIATRIC ONCOLOGY

Screening tools – G8

CGA is time-consuming, and considering older heterogeneity, under situations of limited resources, it is possible to spare some patients full evaluations.

Multiple screening tools – shortened forms of CGA that select patients who need full CGA or not at any given time point – are available.

The G8 is a commonly used screening and validated tool that can be easily performed in approximately five minutes.

G8 does not replace CGA but in clinical practice might already screen patients at risk of frailty, and then rationalise the use of available resources – ideally all patients, and certainly those 80 and above should undergo CGA.
A score of less than 14 is abnormal and correlates with OS.
Comprehensive Geriatric Assessment (CGA) is the standard form of evaluation and follow-up for older patients before and during cancer treatment.

CGA can be defined as “multidimensional interdisciplinary diagnostic process focused on determining a frail older person’s medical, psychological and functional capability, in order to develop a coordinated and integrated plan for treatment and long-term follow-up”.

It identifies problems that are not identified by routine patient history and physical examination.
**GERIATRIC ONCOLOGY**

Comprehensive Geriatric Assessment – Examples of scales/tools

<table>
<thead>
<tr>
<th>Domains</th>
<th>Scales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional status</td>
<td>Eastern Co-operative Oncology Group performance status, Katz basic Activities of Daily Living Scale, Simplified Lawton’s Instrumental Activities of Daily Living Scale</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Charlson comorbidity index</td>
</tr>
<tr>
<td>Medications</td>
<td>Number, type, indication</td>
</tr>
<tr>
<td>Cognitive function</td>
<td>Folstein Mini-Mental State Examination, Schultz-Larsen Mini-Mental State Examination</td>
</tr>
<tr>
<td>Geriatric syndrome</td>
<td>Repeated falls, faecal and/or urinary incontinence</td>
</tr>
<tr>
<td>Depression/mood</td>
<td>Geriatric Depression Scale 5, Emotional questionnaire</td>
</tr>
<tr>
<td>Nutrition</td>
<td>Body mass index</td>
</tr>
<tr>
<td>Mobility</td>
<td>Timed Up and Go test</td>
</tr>
<tr>
<td>Situational assessment</td>
<td>Accessibility of services, mobility, social environment, accessibility of home rooms</td>
</tr>
</tbody>
</table>
**GERIATRIC ONCOLOGY**

**Comprehensive Geriatric Assessment – Comparison of 4 tools of evaluation if frailty**

All tools predict 1-year mortality

<table>
<thead>
<tr>
<th>Classification</th>
<th>Patients, n (%)</th>
<th>Events, n (%)</th>
<th>P-value, log-rank test; trend</th>
<th>HR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balducci</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fit</td>
<td>97 (12.9)</td>
<td>11 (11.3)</td>
<td>&lt;0.001; &lt;0.001</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Vulnerable</td>
<td>113 (14.9)</td>
<td>31 (27.4)</td>
<td>1.91 (0.95, 3.85)</td>
<td></td>
</tr>
<tr>
<td>Frail</td>
<td>544 (72.2)</td>
<td>278 (51.1)</td>
<td>2.94 (1.59, 5.43)</td>
<td></td>
</tr>
<tr>
<td>SIOG1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fit</td>
<td>147 (19.5)</td>
<td>19 (12.9)</td>
<td>1.00 (reference)</td>
<td></td>
</tr>
<tr>
<td>Vulnerable</td>
<td>234 (31.1)</td>
<td>66 (28.2)</td>
<td>1.75 (1.03, 2.97)</td>
<td></td>
</tr>
<tr>
<td>Frail</td>
<td>286 (37.9)</td>
<td>167 (58.4)</td>
<td>3.31 (2.00, 5.50)</td>
<td></td>
</tr>
<tr>
<td>Too sick</td>
<td>87 (11.5)</td>
<td>68 (78.2)</td>
<td>6.12 (3.45, 10.85)</td>
<td></td>
</tr>
<tr>
<td>SIOG2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fit</td>
<td>134 (17.8)</td>
<td>11 (8.2)</td>
<td>1.00 (reference)</td>
<td></td>
</tr>
<tr>
<td>Vulnerable</td>
<td>112 (14.8)</td>
<td>28 (25.0)</td>
<td>2.08 (1.02, 4.22)</td>
<td></td>
</tr>
<tr>
<td>Frail</td>
<td>508 (67.4)</td>
<td>281 (55.3)</td>
<td>3.69 (1.97, 6.89)</td>
<td></td>
</tr>
<tr>
<td>LC typology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relatively healthy</td>
<td>227 (30.1)</td>
<td>27 (11.9)</td>
<td>&lt;0.001; &lt;0.001</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Malnourished</td>
<td>252 (33.4)</td>
<td>110 (43.6)</td>
<td>2.15 (1.34, 3.47)</td>
<td></td>
</tr>
<tr>
<td>Cognitively and/or mood impaired</td>
<td>103 (13.7)</td>
<td>44 (42.7)</td>
<td>2.66 (1.54, 4.61)</td>
<td></td>
</tr>
<tr>
<td>Globally impaired</td>
<td>172 (22.8)</td>
<td>139 (80.8)</td>
<td>4.84 (2.82, 8.31)</td>
<td></td>
</tr>
</tbody>
</table>

All tools predict 6 month hospital admission

<table>
<thead>
<tr>
<th>Classification</th>
<th>Patients, n (%)</th>
<th>Admissions, n (%)</th>
<th>P-value, log-rank test; trend</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No (n=434)</td>
<td>Yes (n=279)</td>
</tr>
<tr>
<td>Balducci</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fit</td>
<td>95 (13.8)</td>
<td>77 (18.4)</td>
<td>18 (6.6)</td>
</tr>
<tr>
<td>Vulnerable</td>
<td>106 (15.4)</td>
<td>70 (16.7)</td>
<td>36 (13.3)</td>
</tr>
<tr>
<td>Frail</td>
<td>489 (70.9)</td>
<td>272 (64.9)</td>
<td>217 (80.1)</td>
</tr>
<tr>
<td>SIOG1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fit</td>
<td>142 (20.6)</td>
<td>115 (27.5)</td>
<td>27 (10.0)</td>
</tr>
<tr>
<td>Vulnerable</td>
<td>213 (30.9)</td>
<td>132 (31.5)</td>
<td>81 (29.9)</td>
</tr>
<tr>
<td>Frail</td>
<td>262 (38.0)</td>
<td>130 (31.0)</td>
<td>132 (48.7)</td>
</tr>
<tr>
<td>Too sick</td>
<td>73 (10.5)</td>
<td>42 (10.0)</td>
<td>31 (11.4)</td>
</tr>
<tr>
<td>SIOG2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fit</td>
<td>134 (19.4)</td>
<td>109 (26.0)</td>
<td>25 (9.2)</td>
</tr>
<tr>
<td>Vulnerable</td>
<td>107 (15.5)</td>
<td>75 (17.9)</td>
<td>32 (11.8)</td>
</tr>
<tr>
<td>Frail</td>
<td>449 (65.1)</td>
<td>235 (56.1)</td>
<td>214 (79.0)</td>
</tr>
<tr>
<td>LC typology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relatively healthy</td>
<td>216 (31.3)</td>
<td>172 (41.1)</td>
<td>47 (16.2)</td>
</tr>
<tr>
<td>Malnourished</td>
<td>233 (33.8)</td>
<td>127 (30.3)</td>
<td>106 (39.1)</td>
</tr>
<tr>
<td>Cognitively and/or mood impaired</td>
<td>87 (12.6)</td>
<td>50 (11.9)</td>
<td>37 (13.7)</td>
</tr>
<tr>
<td>Globally impaired</td>
<td>154 (22.3)</td>
<td>70 (16.7)</td>
<td>84 (31.0)</td>
</tr>
</tbody>
</table>

*aAll Cox models were stratified on in- or outpatient status and adjusted for composite variable, including tumour site and metastatic status, age, year of inclusion, and treatment decision (palliative, curative, or not reported).
Functional status is mainly determined by the capacity of performing:

- **Activities of daily living (ADL):** Concerns basic self care (e.g., bathing, dressing, eating), as well as mobility, balance and continence

- **Instrumental activities of daily living (IADL):** Concerns the ability to perform daily activities, such as shopping, banking, cooking, etc.

Performance status (ECOG or Karnofsky) lacks reliability as a form of functional evaluation in older patients
Quality of Life (QoL) questionnaires may also be a part of functional assessment.

GERIATRIC ONCOLOGY

Comprehensive Geriatric Assessment – Comorbidities

Older patients have a higher incidence of other chronic diseases:

- Chronic diseases that are not immediately-life threatening, but can speed up loss of organ function and limit survival
- More serious diseases, such as heart failure or emphysema, can be important competing causes of morbidity and mortality in an older patient diagnosed with cancer

Therefore, before planning cancer treatment, it is important to estimate the patient’s life expectancy and what are the limits that comorbidities will place on the treatment plan.

Life expectancy is also deeply affected by other domains such as functionality, social status and cognition.
Charlson Index measures risk of death in the next year.

During CGA, comorbidities should be identified, and optimal management initiated.

Comorbid medical conditions might limit cancer treatment options in older patients.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Assigned weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1</td>
</tr>
<tr>
<td>Dementia</td>
<td>1</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>1</td>
</tr>
<tr>
<td>Connective tissue disease</td>
<td>1</td>
</tr>
<tr>
<td>Ulcer disease</td>
<td>1</td>
</tr>
<tr>
<td>Liver disease, mild</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>2</td>
</tr>
<tr>
<td>Renal disease, moderate or severe</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes with end organ damage</td>
<td>2</td>
</tr>
<tr>
<td>Any malignancy</td>
<td>2</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>2</td>
</tr>
<tr>
<td>Malignant lymphoma</td>
<td>2</td>
</tr>
<tr>
<td>Liver disease, moderate or severe</td>
<td>3</td>
</tr>
<tr>
<td>Metastatic solid malignancy</td>
<td>6</td>
</tr>
</tbody>
</table>
Comprehensive Geriatric Assessment – Comorbidities

- Charlson index increase correlates with risk of dying from non-cancer causes

GERIATRIC ONCOLOGY

Comprehensive Geriatric Assessment – Estimating life expectancy

Lee index predicts mortality in 4 and 10 years

It integrates age, comorbidity and cognition and functionality


<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age (years)</td>
<td>60–64</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>65–69</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>70–74</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>75–79</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>80–84</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>≥85</td>
<td>7</td>
</tr>
<tr>
<td>2. Sex (Male/Female)</td>
<td>Male</td>
<td>2</td>
</tr>
<tr>
<td>3. BMI ([703 \times (\text{weight in pounds/height in inches}^2)])</td>
<td>BMI &lt;25</td>
<td>1</td>
</tr>
<tr>
<td>4. Has a doctor ever told you that you have diabetes or high blood sugar? (Y/N)</td>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>5. Has a doctor told you that you have cancer or a malignant tumour, excluding minor skin cancers? (Y/N)</td>
<td>Cancer</td>
<td>2</td>
</tr>
<tr>
<td>6. Do you have a chronic lung disease that limits your usual activities or makes you need oxygen at home? (Y/N)</td>
<td>Lung disease</td>
<td>2</td>
</tr>
<tr>
<td>7. Has a doctor told you that you have congestive heart failure? (Y/N)</td>
<td>Heart failure</td>
<td>2</td>
</tr>
<tr>
<td>8. Have you smoked cigarettes in the past week? (Y/N)</td>
<td>Smoke</td>
<td>2</td>
</tr>
<tr>
<td>9. Because of a health or memory problem do you have any difficulty with bathing or showering? (Y/N)</td>
<td>Bathing</td>
<td>2</td>
</tr>
<tr>
<td>10. Because of a health or memory problem, do you have any difficulty with managing your money—such as paying your bills and keeping track of expenses? (Y/N)</td>
<td>Finances</td>
<td>2</td>
</tr>
<tr>
<td>11. Because of a health problem do you have any difficulty with walking several blocks? (Y/N)</td>
<td>Walking</td>
<td>2</td>
</tr>
<tr>
<td>12. Because of a health problem do you have any difficulty with pulling or pushing large objects like a living room chair? (Y/N)</td>
<td>Push or pull</td>
<td>1</td>
</tr>
</tbody>
</table>
Cognition in cancer patients is crucial for treatment compliance.

Patients need to be able to understand information given, prognosis and treatment options.

When cognitive dysfunction is suspected, specific screening tools such as mini-Cog can be applied – caregivers can also be a valuable source of additional information.

Ideally, patients need to be able to make decisions independently.

Older patients may have cognitive dysfunction that partly or completely precludes decision making – and in such cases family members, caregivers and geriatricians who are familiar with the patient may give valuable information.

Cognitive dysfunction should be carefully differentiated from depression and hearing problems.
Older persons may have different priorities when making decisions – such as maintaining functionality and independence – that may be to them more important than living longer.

Establishing these priorities clearly is a critical aspect of defining cancer care.

Ideally, patients need to be able to make decisions independently.

Older patients may have cognitive dysfunction that partly or completely precludes decision making – and in such cases family members, caregivers and geriatricians who are familiar with the patient may give valuable information.

Don’t forget that family members and caregiver (even geriatricians) can lose objectivity and provide information based on their needs and not the patient’s.
Multiple factors affect cognition of cancer patients

Cancer diagnosis and cancer therapeutics
- Chemotherapy treatments
- Hormonal therapies

Psychological status
- Anxiety
- Depression
- Distress
- Fatigue

Cognitive functioning
- Objective performances
- Subjective complaints

Treatment cancer impact
- Inflammation
- Fatigue
- Sleep difficulty / hypersomnia
- Chemic-induced menopause

Genetic variation
- ApoE

Comorbidity
- Vascular risk factors
- Cardiovascular disease
- Diabetes

Lifestyle
- Physical activity
- Diet / nutrition
- Smoking
- Alcohol

Sociodemographics
- Gender
- Education
- Cognitive reserve

Biological factors
- Cell senescence
- Inflammation
- DNA damage
- Oxidative stress
- Decrease in telomeres length

Malnourishment can be defined as a state of nutrition in which a deficiency or imbalance of energy, protein, and other nutrients causes measurable adverse effects on tissue and/or body form. In older patients, three different forms can be present separately or together:

- **Wasting**: loss of weight that is involuntary and due to low nutritional intake
- **Cachexia**: involuntary loss of body mass caused by catabolism
- **Sarcopenia**: involuntary loss of muscle mass and muscle function, which can be disease related or not in older patients

Malnutrition is a significant problem among older persons, specially those with cancer

General population data using MNA

Causes for anorexia in older patients

↓ Energy expenditure

↓ Exercise

Physiological changes with aging
- Hormonal
- Cytokines
- ↓ Taste and smell
- ↓ Changes in GI tract

Pathological changes with aging
- Medical
- Drugs
- Physiological
- Social
GERIATRIC ONCOLOGY
Comprehensive Geriatric Assessment – Nutritional status

Malnutrition impacts chemotherapy toxicity:
- Weight loss
- Hypoalbuminemia
- Low body nitrogen
- Sarcopenia
- Low BMI

Malnutrition is also an independent negative prognostic factor
Link between old age and depression

- Long-standing vulnerabilities (e.g. cognitive style)
- Stressful life events and loss of social roles
- Changes in health, physical ability, or cognitive ability
- Limitation of activities
- Self-critical cognitions
- Low rate of positive outcomes

Depression

Cancer patients of all ages profit from extensive social support

Older patients are likely to have less social support due to widowhood, death of friends and other family members

Social support is especially critical considering the complexity of undergoing cancer treatment – correctly taking medications at home, keeping appointments, bringing exams and seeking assistance in case of complications

Abuse of older persons (physical, economic and emotional) also remains a problem, as well as the disempowerment of independent patients by their family members after a diagnosis of cancer
GERIATRIC ONCOLOGY

Comprehensive Geriatric Assessment – Medication use

Older patients often use multiple drugs besides those connected to cancer treatment, putting them at risk of polypharmacy.

Polypharmacy may be defined in different ways but is at its core the combination of number of medication and utility of medications.

Older persons tend to accumulate both physicians and treatments.

E.g.: A 75-year-old man with metastatic lung cancer takes statins to control his cholesterol.
What problems can polypharmacy cause?

Medication-related problems associated with polypharmacy

- Adverse drug reactions
- Duplication of therapy
- Adverse drug-drug interactions
- Adverse drug-disease interactions
- Adherence to treatment
- Cost
GERIATRIC ONCOLOGY

Comprehensive Geriatric Assessment – Medication questions

Is there a proper indication for each drug?
Is the medication proving effective?
Is the medication causing side effects?
Is the dose appropriate?
Is there potential for significant interactions?
Is there potential of interaction with planned cancer treatment?
Can a drug affect the tumour?
Does the patient adhere to the treatment plan?
Are there other conditions that need treatment?

The concept of geriatric syndrome differ from those of disease and syndrome
GERIATRIC ONCOLOGY
Chemotherapy side effects in older patients

Risk of chemotherapy side effects might be increased in older patients

Older patients can expect a higher rate of neutropenia, fatigue, cardiac toxicity and neuropathy than younger patients

Older patients more often need dose reductions, delays and permanent interruptions than younger patients

However, older patients benefit from standard chemotherapy regimens, including doublets in breast cancer and lung cancer, if carefully selected and followed
GERIATRIC ONCOLOGY
Chemotherapy toxicity in older patients – Prediction tools

Two scores developed in cancer population to predict treatment complications based on data generated by CGA

Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score

Cancer and Age Research Group (CARG) Score

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

Prospective study on patients seventy or older (N=331)

Estimates grade 3-4 CT toxicity

Score composed of a haematologic and non-haematologic variables

Divides patients into 4 groups: low, medium-low, medium-high and high

Internal validation (n=187)

## Geriatric Oncology

Chemotherapy side effects in older patients – CRASH score

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td><strong>Haematologic score</strong></td>
<td></td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>≤72</td>
</tr>
<tr>
<td>IADL</td>
<td>26–29</td>
</tr>
<tr>
<td>LDH (if ULN 618 U/L; otherwise, 0.74/L*ULN)</td>
<td>0–459</td>
</tr>
<tr>
<td>Chemotox</td>
<td>0–0.44</td>
</tr>
<tr>
<td><strong>Nonhaematologic score</strong></td>
<td></td>
</tr>
<tr>
<td>ECOG PS</td>
<td>0</td>
</tr>
<tr>
<td>MMS</td>
<td>30</td>
</tr>
<tr>
<td>MNA</td>
<td>28–30</td>
</tr>
<tr>
<td>Chemotox</td>
<td>0–0.44</td>
</tr>
</tbody>
</table>

GERIATRIC ONCOLOGY
Chemotherapy side effects in older patients – CRASH score

GERIATRIC ONCOLOGY

Chemotherapy side effects in elderly patients – CARG

Predicting chemotherapy toxicity in older adults with cancer: A prospective multicentre study

- 65 or older
- Diagnosis of cancer
- To start a new chemotherapy regimen

CGA → Chemotherapy with toxicity grading at each visit → Post-chemo CGA

GERIATRIC ONCOLOGY
Predictors of CT toxicity – CARG score

- Age ≥72 years
- GI/GU cancer
- Standard dose
- Polychemotherapy
- Haemoglobin (male: <11, female: <10)
- Creatinine clearance (Jelliffe-ideal weight)
- Fall(s) in last 6 months
- Hearing impairment (fair or worse)
- Limited in walking 1 block
- Assistance required in medication intake (IADL)
- Decreased social activity

GERIATRIC ONCOLOGY

CARG score

Estimates risk of grade 3-5 toxicity

Categorises patients into 3 risk groups
  – low, intermediate and high

External validation

GERIATRIC ONCOLOGY

Evidence for the benefit of interventions: GAIN Trial – Study design

Reproduced with permission from Dr Daneng Li, et al.
**GERIATRIC ONCOLOGY**

Evidence for the benefit of interventions: GAIN Trial (N=605)

<table>
<thead>
<tr>
<th>Toxic effects</th>
<th>GAIN (n=402)</th>
<th>SOC (n=203)</th>
<th>Total (N=605)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with grade 3 or higher chemotherapy-related toxic effects</td>
<td>203 (50.5) [45.6, 55.4]</td>
<td>123 (60.6) [53.9, 67.3]</td>
<td>326 (53.9) [49.9, 57.9]</td>
<td>0.02</td>
</tr>
<tr>
<td>Haematologic only</td>
<td>45 (11.2) [8.1, 14.3]</td>
<td>39 (19.2) [13.8, 24.6]</td>
<td>84 (13.9) [11.1, 16.6]</td>
<td>0.003</td>
</tr>
<tr>
<td>Non-haematologic only</td>
<td>74 (18.4) [14.6, 22.2]</td>
<td>54 (26.6) [20.5, 32.7]</td>
<td>128 (21.2) [17.9, 24.4]</td>
<td>0.007</td>
</tr>
<tr>
<td>Both haematologic and non-haematologic</td>
<td>84 (20.9) [16.9, 24.9]</td>
<td>30 (14.8) [9.9, 19.7]</td>
<td>114 (18.8) [15.7, 22.0]</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Implementation of geriatric assessment and intervention reduced grade 3 or higher adverse events related to chemotherapy

### GERIATRIC ONCOLOGY

Evidence for the benefit of interventions: GAIN Trial (N=605)

**Secondary outcomes comparisons between GAIN and SOC arms**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>GAIN (n=402)</th>
<th>SOC (n=203)</th>
<th>Total (n=605)</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute change in AD status&lt;sup&gt;b&lt;/sup&gt;</td>
<td>114 (28.4) [24.0, 32.8]</td>
<td>27 (13.3) [8.6, 18.0]</td>
<td>141 (23.3) [19.9, 26.7]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency department visit</td>
<td>110 (27.4) [23.0, 31.7]</td>
<td>62 (30.5) [24.2, 36.9]</td>
<td>172 (28.4) [24.8, 32.0]</td>
<td>0.41</td>
</tr>
<tr>
<td>Unplanned hospitalisation</td>
<td>89 (22.1) [18.1, 26.2]</td>
<td>39 (19.2) [13.8, 24.6]</td>
<td>128 (21.2) [17.9, 24.4]</td>
<td>0.41</td>
</tr>
<tr>
<td>Average length of stay, days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>5.9 (4.2)</td>
<td>6.8 (5.6)</td>
<td>6.2 (4.7)</td>
<td>NA</td>
</tr>
<tr>
<td>Median (range)</td>
<td>5 (1–23)</td>
<td>5 (1–26)</td>
<td>5 (1, 26)</td>
<td>0.60&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Unplanned readmission</td>
<td>17 (19.1) [10.9, 27.3]</td>
<td>8 (20.5) [7.8, 33.2]</td>
<td>25 (19.5) [12.7, 26.4]</td>
<td>0.85</td>
</tr>
<tr>
<td>Early chemotherapy discontinuation</td>
<td>216 (53.7) [48.9, 58.6]</td>
<td>118 (58.1) [51.3, 64.9]</td>
<td>334 (55.2) [51.2, 59.2]</td>
<td>0.30</td>
</tr>
<tr>
<td>Chemotherapy dose modifications&lt;sup&gt;d&lt;/sup&gt;</td>
<td>218 (54.2) [49.4, 59.1]</td>
<td>95 (46.8) [39.9, 53.7]</td>
<td>313 (51.7) [47.8, 55.7]</td>
<td>0.08</td>
</tr>
</tbody>
</table>

A : P values were obtained from X2 test unless otherwise noted  
B : Absolute change in AD status reflects the change from no AD at baseline to having an AD at the end of primary/secondary outcome follow-up  
C : P value was obtained from Kruskal-Wallis test  
D : dose modifications: reductions or delays

AD, Advance directive  
GERIATRIC ONCOLOGY
Evidence for the benefit of interventions: GAP 70+

Study schema: Geriatric assessment for patients 70+

GA Intervention Arm
Oncology physician provided with GA summary and GA-guided recommendations for each enrolled participant prior to starting a new chemotherapy/agent(s) with similar prevalence of toxicity

Endpoints
- Clinician-rated grade 3-5 toxicity
- Survival at 6 months
- Treatment decisions
- Functional and physical decline
- Patient-reported toxicities

Presented at ASCO 2020; with permission from Dr Supriya Mohile.
GERIATRIC ONCOLOGY
Evidence for the benefit of interventions: GAP 70+

Any Grade 3-5 CTCAE toxicity in 3 months

- Any Grade 3-5 toxicity
  - Adjusted Risk Ratio: 0.74
  - 95% CI: 0.63, 0.87 (P<0.01)
  - Clustering effect: P=0.15

- Any Grade 3-5 haematologic toxicity
  - Adjusted Risk Ratio: 0.85
  - 95% CI: 0.69, 1.05 (P=0.13)
  - Clustering effect: P=0.30

- Any Grade 3-5 non-haematologic toxicity
  - Adjusted Risk Ratio: 0.73
  - 95% CI: 0.53, 0.996 (P=0.047)
  - Clustering effect: P<0.01

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GERIATRIC ONCOLOGY

Evidence for the benefit of interventions: GAP 70+

Treatment intensity

- Adjusted Risk Ratio = 1.37
  95% CI: 1.06, 1.76 (P=0.016)
  Clustering effect: P=0.03

- Adjusted Risk Ratio = 0.85
  95% CI: 0.67, 1.08 (P=0.190)
  Clustering effect: P<0.01

Reduced dose intensity at Cycle 1

Dose modification at 3 months related to toxicity

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**GERIATRIC ONCOLOGY**

Evidence for the benefit of interventions: INTEGRATE study

- Age ≥70 years
- Solid tumours
- For chemo-/ immuno-/ targeted therapy
- No treatment ≤3 months

N=154

**Integrated oncogeriatric care**
n=76

**Usual care**
n=78

**Primary:** HRQOL

**Secondary:**
- Healthcare utilisation
- Treatment delivery
- Function
- Institutionalisation
- Mood
- Nutrition
- Health utility
- Survival

GERIATRIC ONCOLOGY
Evidence for the benefit of interventions: INTEGRATE study

Primary outcome: Health-related quality of life

Intervention group reported significantly better scores than usual care group in the following other HRQOL domains:

- Functioning (physical, role, social)
- Mobility
- Burden of illness
- Future worries

Functional benefits were maximal around Week 18, then reduced by Week 24

Benefits in the social functioning, burden of illness and future worries domains persisted (to end of study at Week 24)

GERIATRIC ONCOLOGY
Evidence for the benefit of interventions: INTEGRATE study

Secondary outcomes: Hospitalisation
39% fewer emergency presentations
- Incidence rate ratio (IRR)* 0.61 (95% CI: 0.46, 0.77; P=0.007)
- −1.3 emergency presentations per person-year
41% fewer unplanned hospital admissions
- IRR* 0.59 (95% CI: 0.41, 0.86; P<0.001)
- −1.2 admissions per person-year
24% fewer unplanned hospital overnight bed-days
- IRR* 0.76 (95% CI: 0.68, 0.85; P<0.001)
- −7.0 days per person-year

*Adjusted for age, gender, ECOG-PS, cancer type and treatment intent.
GERIATRIC ONCOLOGY
Evidence for the benefit of interventions: INTEGRATE study

Secondary outcomes: Treatment delivery
Lower early treatment discontinuation due to adverse events (32.9% vs. 53.2%; P=0.01)
  ◆ Driven by fewer discontinuations due to toxicity

No difference in treatment reduction, escalation or delay

Clinical trials are the main driver of improvement in cancer treatment outcomes.

As the proportion of older patients increases for a large number of solid tumours, it becomes critical to ensure that older patients participate in clinical trials.

Historically, however, participation has been low in proportion to the actual number of older patients for multiple reasons.

Clinical trials targeting older and frail patients are necessary, and also for leveraging real-world data.

Geriatric Oncology

Participation of older patients in clinical trials

A study of the participation of older patients in alliance trials

GERIATRIC ONCOLOGY

Participation of older patients in clinical trials

Present challenges in gaining informed consent
Multiple comorbid conditions may pose challenges in outcomes assessment
Polypharmacy may lead to drug-drug interactions
Challenges in compliance with clinical study procedures
May necessitate age-relevant formulations and packing
Fear of failure due to confounding behaviour of the drug in older patients
Sponsors may incur higher cost for medical management and compensation
Institutional and logistic problems
May need supportive care
Investigator’s preferences and perceived difficulties in screening
Protocol restrictions with exclusion criteria on age or age-related comorbidities

## GERIATRIC ONCOLOGY

### Participation of older patients in clinical trials

#### Beyond OS, iDFS and PFS for older patients: End-points that include tolerability

<table>
<thead>
<tr>
<th>End Point</th>
<th>Definition</th>
<th>Current Situation</th>
<th>Pro</th>
<th>Con</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TFFS and TTF:</strong> time or proportion</td>
<td>TFFS is time elapsing between random assignment and early treatment discontinuation because of any reason (including disease progression, treatment toxicity, early death), disease progression, death (resulting from any cause), or any other event of interest; TTF is similar, but death resulting from any other cause is not considered</td>
<td>Often used in addition to OS</td>
<td>Integrates efficacy and toxicity</td>
<td>Difficult to distinguish between efficacy and toxicity (e.g., toxic but effective)</td>
</tr>
<tr>
<td>QoL-related endpoints: Level at specified timepoint or time until deterioration compared with baseline</td>
<td>Evaluation of evolution of functioning and (in)dependence through validated instruments during course of disease/treatment/study</td>
<td>Rarely measured in oncology trials but crucial to include</td>
<td>Main contributor to QoL in elderly patients with cancer</td>
<td>No general consensus on optimal measurement or clinically relevant cutoffs determining whether therapy is worthwhile</td>
</tr>
</tbody>
</table>

DSS, disease-specific survival; TFFS, treatment failure–free survival; TTF, time to treatment failure.

GERIATRIC ONCOLOGY

Concluding remarks

Older patients will dominate future oncology practice

More initiatives are necessary to educate oncologists and integrate geriatrics into usual oncology practice and services

Critically, more older-centred studies with appropriate endpoints are necessary to provide the basis for more specific treatment standards

Together this will allow to close the gap that currently exists between younger and older patients, and will lead to better outcomes
THANK YOU!