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**NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)**

# Older Adult Oncology

Version 1.2025 — December 9, 2024

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# NCCN Guidelines Version 1.2025

## Older Adult Oncology

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# NCCN Guidelines Version 1.2025

## Older Adult Oncology

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**NCCN Categories of Evidence and Consensus:** All recommendations are category 2A unless otherwise indicated.

See [NCCN Categories of Evidence and Consensus](#).

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**Updates in Version 1.2025 of the NCCN Guidelines for Older Adult Oncology from Version 1.2024 include:**

**General**

- References were updated throughout the guidelines.
- Patient's 'goals and values' or 'goals and objectives' modified to 'values and goals'.
- 'Geriatric Assessment' modified to 'Geriatric Assessment and Interventions'.
- 'His or her' modified to 'their'.

**OAO-1**

- Definition of the Older Adult Oncology Population

► 1st bullet modified: There is no chronologic age threshold to define an older adult. *The guidelines herein focus on physiologic age and function to define the older adult oncology population. (Note: Some consider individuals aged ≥65 years to be and over is generally considered the chronologic definition of an older adults, as this is the usual age of eligibility for Medicare benefits.) The guidelines herein focus on physiologic age and function to define the older adult oncology population.*

**OAO-2**

- Approach To Shared Decision-making In The Older Adult Prior To Cancer-Specific Treatment

► Bottom pathway, 1st bullet added: Assess the patient's preferred role in decision-making  
► Footnote b modified: 'For example' added.  
► Footnote f added: This can include the patient's preference for their, their caregivers, and/or their provider's role in shared decision-making.  
► Footnote g added: These should be obtained for all patients at the time of treatment initiation.

**OAO-4**

- Considerations For Older Adults Undergoing Cancer-Specific Treatment

► General Considerations

◊ 3rd bullet added: Offer a shared decision-making tool/framework to guide treatment decisions.  
◊ 5th bullet added: Older adult cancer care is complex; thus, use of multidisciplinary care teams and testing of different models of care delivery can be strategies for efficient care delivery.  
◊ 6th bullet added: Observation may be an appropriate approach in particular clinical scenarios, and may align with patient's preference.  
◊ 7th bullet, 1st sub bullet modified: What Matters ~~most~~: Care is aligned with individual *values and goals and preferences*.

► Specific Considerations by Treatment Type

◊ Surgery,

– 1st bullet modified: Chronologic age is not the primary consideration for surgical risk; all older adults undergoing surgery should undergo an assessment for components of frailty including comorbidities, cognition, mobility, functional status, and nutrition. *For patients who are at high risk with multimorbidities and complex health conditions, consider multidisciplinary input with geriatric expertise.*  
– 5th bullet added: The surgical plan can be altered as necessary to consider non-surgical or less morbid options.



Updates in Version 1.2025 of the NCCN Guidelines for Older Adult Oncology from Version 1.2024 include:

### OAO-5

- Considerations For Older Adults Undergoing Cancer-Specific Treatment

- ▶ Radiation therapy (RT)

◊ 3rd bullet modified: Use caution with concurrent chemoradiation therapy. Dose or sequence modification of chemotherapy or chemoradiation, additional supportive services, and more frequent monitoring may be necessary. See disease-specific NCCN Guidelines for Treatment by Cancer Type.

◊ 5th bullet modified: Local ablative RT should be considered as an adjunct or alternative to systemic therapy in older adults with oligometastatic disease.

- ▶ Chemotherapy

◊ 1st bullet modified: Consider use of chemotherapy toxicity risk calculators where validated (predominantly solid tumors) to estimate toxicity and determine dose adjustments, additional supportive services, more frequent monitoring, and geriatric assessment as necessary.

### OAO-6

- Considerations For Older Adults Undergoing Cancer-Specific Treatment

- ▶ Immunotherapy

◊ 1st bullet modified: Older adults are underrepresented in clinical trials studying immunotherapy across multiple cancers. Most subgroup analyses and retrospective studies report a similar clinical benefit in older and younger patients, with some concerns for increase in toxicity rates. Overall, studies show that older patients have similar clinical benefit; however, closer and more aggressive follow-up may be needed related to toxicities.

◊ 2nd bullet added: See disease-specific NCCN Guidelines for Treatment by Cancer Type and NCCN Guidelines for the Management of Immunotherapy-Related Toxicities.

- ▶ Targeted therapy

◊ 1st bullet added: Similar clinical benefit has been observed with these therapies in older patients compared to younger adults. However, side effects are not as well understood; thus, patients may require greater supervision with consideration of earlier and more aggressive management of side effects/toxicities.

◊ 2nd bullet added: Oral targeted therapy should be closely monitored for adherence.

- ▶ Chimeric antigen receptor (CAR) T-cell therapy changed to Cellular therapy/T-cell engagers

◊ 1st bullet modified: Chimeric antigen receptor (CAR) T-cell therapy has been shown to be an effective therapeutic option for older adults with similar response rates as younger adults, and age should not be an absolute contraindication for the use of these therapies for these patients. However, older adults, especially those who are frail or unfit, may have a higher incidence of neurologic toxicities and require close monitoring (NCCN Guidelines for the Management of Immunotherapy-Related Toxicities).

### OAO-7

- Management Of Common Side Effects In Older Adults Undergoing Cancer-Specific Treatment

▶ 1st bullet added: An older patient may have less reserve to manage toxicities. Complications may be more clinically significant and may require more intense surveillance.

▶ 2nd bullet added: Consider that toxicities may have immediate or even long-term effects that are more significant.

▶ 4th row added: Infection/immunosuppression

▶ Neurotoxicity row, 5th bullet added: Consider polypharmacy (2023 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults) (OAO-D 5 of 10).

▶ Footnote j added: Assess for polypharmacy and use of non-prescribed agents as they can enhance these side effects (2023 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults) (OAO-D 8 of 10). (Also OAO-8)

**CONTINUED**  
**UPDATES**



Updates in Version 1.2025 of the NCCN Guidelines for Older Adult Oncology from Version 1.2024 include:

### OAO-8

- Management Of Common Side Effects In Older Adults Undergoing Cancer-Specific Treatment
  - ▶ Renal toxicity row, 1st bullet modified: Serum creatinine is not a good indicator of renal function in older adults. Calculation of estimated creatinine clearance is recommended to assess renal function and adjust dose to reduce systemic toxicity (OAO-D 2 of 10).

### OAO-B 1 OF 2

- Page heading modified: *Guidance For The Optimization Of Optimizing Communication With Older Adults*
  - ▶ 2nd sub heading modified: Written materials (eg, *after visit summaries*)
    - ◊ 1st bullet added: Offer written instructions after the appointment

### OAO-B 2 OF 2

- ▶ New section added: Digital communication/Telehealth/Digital health

### OAO-C 1 OF 2

- Page heading modified: *Geriatric Screening Tools Identification Of Patients Requiring Geriatric Assessment*
  - ▶ 1st bullet modified: Geriatric screening tools are used to identify older adults with cancer who would benefit from a geriatric assessment (GA) (OAO-D 1 of 10). *All are self-reported and any of these tools can be used. Choose one.*
  - ▶ Footnote a added: For more information, see Discussion.
  - ▶ Footnote b added: No evidence exists for superiority of these tools.

### OAO-D 1 OF 10

- Section heading modified: *Geriatric Assessment (GA) And Interventions*
  - ▶ Reasons to Perform GA
    - ◊ 6th bullet modified: GA can be helpful in improving communication of *aging-related concerns*.
  - ▶ Collaboration Between Geriatric Trained Clinician and Oncologist in the Care of an Older Patient with Cancer
    - ◊ 4th bullet added: Polypharmacy evaluation
    - ◊ 5th bullet added: Presence of geriatric syndromes such as frailty, osteoporosis, depression, pressure ulcers, urinary incontinence, neglect or abuse, failure to thrive, or sarcopenia
  - ▶ Medication Management section removed

### OAO-D 2 OF 10

- ▶ 1st bullet removed: GA 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 and/or patient to perform these assessments as listed below.
- ▶ 2nd bullet modified: Patient's *wishes/values and goals and objectives* with regard to *their his/her cancer diagnosis can be used to inform treatment, decision planning, dose adjustments, schedule changes, etc* 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.
- ▶ 1st domain modified: Self-Reported *Mobility and Function and Mobility*
- ▶ Objective Function and Mobility row, Tools reordered.
- ▶ Additional Assessments/Potential Interventions, 5th bullet added: Evaluate medication use (consider orthostasis and overtreatment of hypertension [hypotension] and diabetes [hypoglycemia])
- ▶ Footnote removed: Adapted with permission from Mohile SG, Velarde C, Hurria A, et al. J Natl Compr Canc Netw 2015;13:1120-1130. (Also for OAO-D 3, OAO-D 4 and OAO-D 5)

**CONTINUED**  
**UPDATES**



Updates in Version 1.2025 of the NCCN Guidelines for Older Adult Oncology from Version 1.2024 include:

### OAO-D 3 OF 10

- Comorbidity
  - ▶ Additional Assessments/Potential Interventions
    - ◊ 4th bullet added: Consider comorbidities when deciding on treatment
- Social Functioning and Support row
  - ▶ Assessment Tools/Description, 1st row
    - ◊ 1st bullet modified: Measure the availability of social support, **and** engagement in physical or social activities, **and** loneliness/social isolation
      - 2nd sub bullet added: UCLA 3-Item Loneliness Scale

### OAO-D 5 OF 10

- Nutrition row
  - ▶ Guide to Nutritional Intervention from NCI Nutrition in Cancer Care (PDQ) moved from Assessment Tools/Description column to Additional Assessments/Potential Interventions column
  - ▶ Additional Assessments/Potential Interventions
    - ◊ 9th bullet added: Provide nutrition education for management of nutrition impact symptoms
- Medication Management row changed to Medications
  - ▶ Assessment Tools/Description
    - ◊ 1st row modified: Prescription and *non-prescription over-the-counter medications or substances list*
    - ▶ Additional Assessments/Potential Interventions
      - ◊ 2nd bullet added: Evaluate for opioid and substance abuse

### OAO-D 6 OF 10

- Functional Status
  - ▶ 5th bullet, 3rd sub bullet, 3rd sub sub bullet modified: Checking vitamin D levels and supplementing vitamin D if low and *assess bone mineral density (BMD)*
- Socioeconomic Considerations
  - ▶ 4th bullet added: Loneliness and isolation (UCLA 3-Item Loneliness Scale)

### OAO-D 8 OF 10

- Heading modified: Medications Management

### OAO-E

- Falls Assessment And Interventions
  - ▶ Environmental hazards row, 2nd bullet modified: Educate patients to reduce risk (<https://www.cdc.gov/steady/pdf/STEADI-Brochure-CheckForSafety-508.pdf>) (<http://www.cdc.gov/HomeandRecreationalSafety/Falls/CheckListForSafety.html>)

### OAO-F 3 OF 4

- Assessment of Cognitive Function
- Screening Tool row
  - ▶ Mild Cognitive Impairment column modified: Clinical interview with Cognitive (Mini-Cog), MMSE, MoCA, SLUMS, and functional (ADL/IADL, OAO-D, 2 of 10) assessment
  - ▶ Dementia column modified: Clinical interview with Cognitive (Mini-Cog), MMSE, MoCA, SLUMS, and functional (ADL/IADL, OAO-D, 2 of 10) assessment

**CONTINUED**  
**UPDATES**



**Updates in Version 1.2025 of the NCCN Guidelines for Older Adult Oncology from Version 1.2024 include:**

**OAO-H 3 OF 7**

- Medications Commonly Used For Supportive Care That Are Of Concern In Older Patients
  - ▶ First-generation antihistamines
    - ◊ Alternative(s)
      - 1st bullet modified: Consider second-generation antihistamines (ie, cetirizine, desloratadine, *loratadine*, fexofenadine, levocetirizine), intranasal antihistamines, intranasal anticholinergics, or leukotriene inhibitors.

**OAO-H 5 OF 7**

- Medications Commonly Used For Supportive Care That Are Of Concern In Older Patients
  - ▶ Antipsychotics
    - ◊ Recommendation
      - 3rd bullet modified: May be appropriate for short-term management of delirium *or for patients with severe agitation, which will result in interruption of essential medical therapies or poses a danger for self-injury; or for those with distressing psychotic symptoms (eg, hallucinations, delusions).*

**OAO-H 6 OF 7**

- Medications Commonly Used For Supportive Care That Are Of Concern In Older Patients
  - ▶ Opioids
    - ◊ Therapeutic Class/Medication(s)
      - 9th bullet added: buprenorphine
    - ◊ Recommendation
      - 6th bullet added: Buprenorphine is the preferred agent in older adults requiring long-acting opioids.

**OAO-K**

- New sections added:
  - ▶ Considerations For Caregivers Of Older Adults With Cancer
  - ▶ Approach To Assessing Caregiver Status



## DEFINITION AND PURPOSE

### Definition of the Older Adult Oncology Population

- There is no chronologic age threshold to define an older adult. The guidelines herein focus on physiologic age and function to define the older adult oncology population. (Note: Some consider individuals aged  $\geq 65$  years to be older adults, as this is the usual age of eligibility for Medicare benefits.)

### Purpose of the NCCN Guidelines for Older Adult Oncology

- There are unique issues to consider when caring for an older adult with cancer.
- The biologic characteristics of certain cancers and their responsiveness to therapy may be different in older patients compared to their younger counterparts.
- The psychologic and psychosocial changes associated with aging may impact an older adult's ability to tolerate cancer therapy and should be considered in the treatment decision-making process. See [NCCN Guidelines for Distress Management](#).
- Advanced age alone should not be the only criterion to preclude effective treatment that could improve quality of life (QOL) or lead to a survival benefit in older patients.
- Multidisciplinary team management, patient-specific treatment approach with shared decision-making, and palliative/supportive care for symptom management should be an integral part of cancer care in older adults. See [NCCN Guidelines for Supportive Care](#) and [NCCN Guidelines for Palliative Care](#).
- These age-related issues form the basis for the development of NCCN Guidelines for Older Adult Oncology that address special considerations in older patients with cancer.

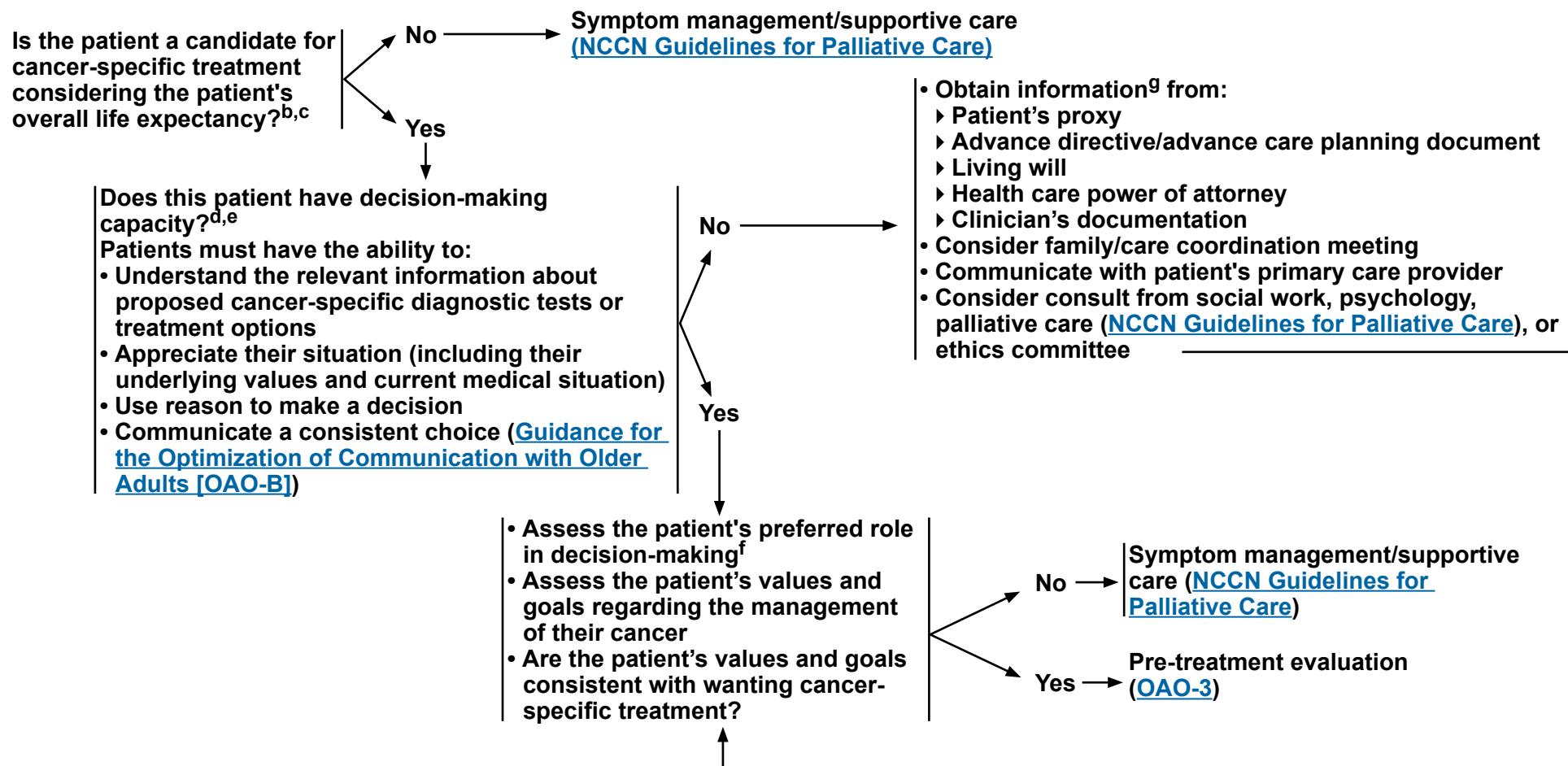
Note: All recommendations are category 2A unless otherwise indicated.



# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### APPROACH TO SHARED DECISION-MAKING IN THE OLDER ADULT PRIOR TO CANCER-SPECIFIC TREATMENT<sup>a</sup>



<sup>a</sup> Assessment of the patient's values and goals with regard to 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.

<sup>b</sup> For example: life expectancy calculators are available at [www.eprognosis.com](http://www.eprognosis.com). Note that these calculators are used to determine anticipated life expectancy (independent of the cancer). They could be utilized in clinical decision-making to weigh whether the cancer is likely to shorten the patient's life expectancy or whether the patient is likely to become symptomatic from cancer during anticipated life expectancy.

<sup>c</sup> [Life Expectancy of General Population \(OAO-A\)](#).

<sup>d</sup> Sessums LL, et al. JAMA 2011;306:420-427.

<sup>e</sup> McKoy JM, et al. J Natl Compr Canc Netw 2014;12:138-144.

<sup>f</sup> This can include the patient's preference for their, their caregivers, and/or their provider's role in shared decision-making.

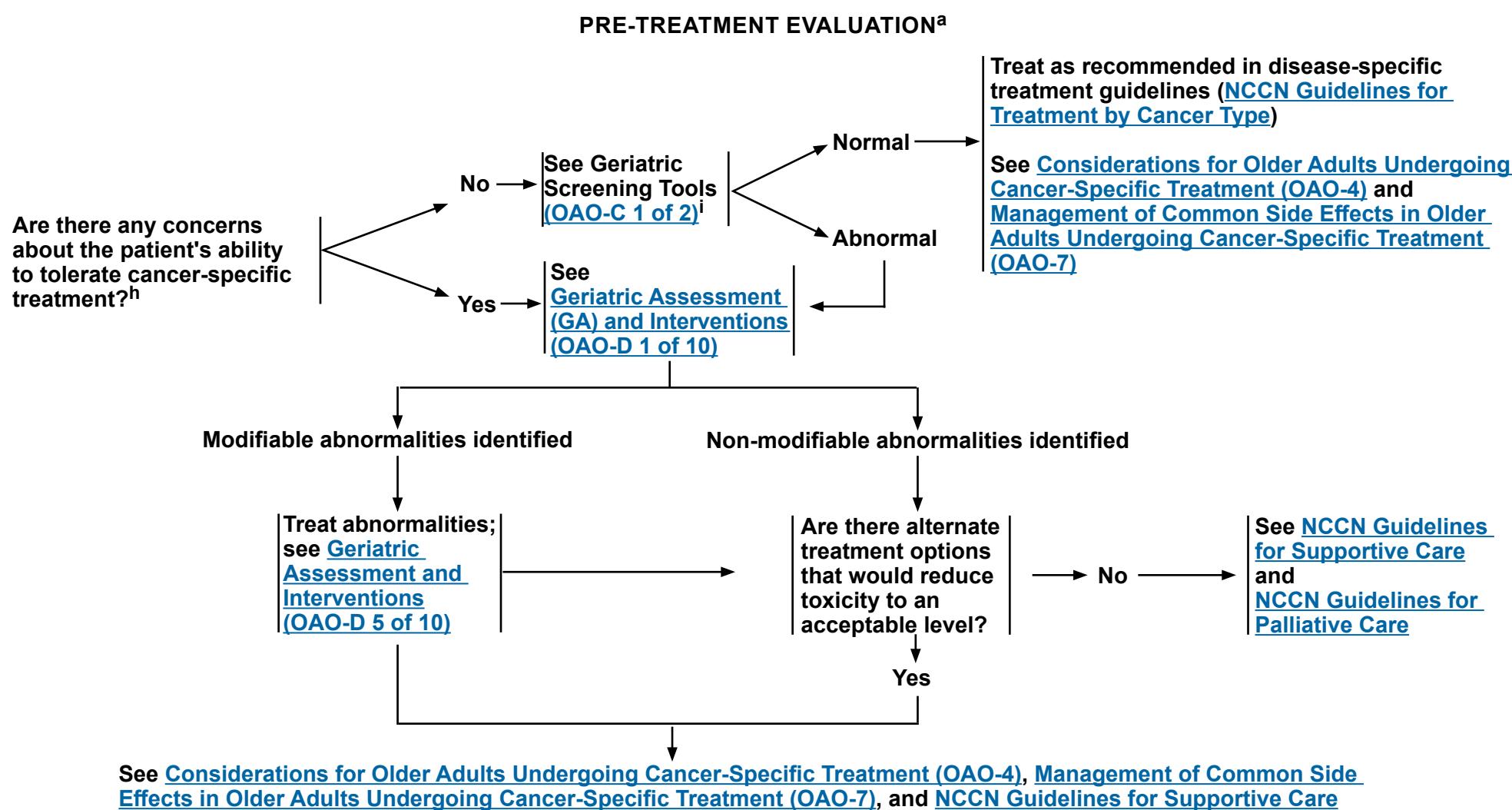
<sup>g</sup> These should be obtained for all patients at the time of treatment initiation.

**Note:** All recommendations are category 2A unless otherwise indicated.



# NCCN Guidelines Version 1.2025

## Older Adult Oncology



<sup>a</sup> Assessment of the patient's values and goals with regard to 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 (OAO-2).

<sup>h</sup> Concerns can come from the patient, family, or clinician and can be related to the patient's performance status and/or comorbidities.

<sup>i</sup> Multiple screening tools have been tested and validated in this setting. Selected geriatric screening tools that have been used to determine if a GA 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.



## CONSIDERATIONS FOR OLDER ADULTS UNDERGOING CANCER-SPECIFIC TREATMENT<sup>a</sup>

### General Considerations

- Patient's values and goals should be assessed in context with life expectancy; comorbidities; cognitive, functional, psychologic/psychosocial, and nutritional status; aggressiveness of the disease; and treatment approach ([OAO-3](#)).
- There are data to suggest correlation between low social support and a higher risk for mortality. In patients with low levels of social support, consider referral to social work and/or case management to explore home supports and community resources.
- Offer a shared decision-making tool/framework to guide treatment decisions.
- Multidisciplinary team management, patient-specific treatment approach with shared decision-making, and palliative/supportive care for symptom management should be an integral part of cancer care in older adults. See [NCCN Guidelines for Supportive Care](#) and [NCCN Guidelines for Palliative Care](#).
- Older adult cancer care is complex; thus, use of multidisciplinary care teams and testing of different models of care delivery can be strategies for efficient care delivery.
- Observation may be an appropriate approach in particular clinical scenarios, and may align with patient's preference.
- *Age-Friendly Health Systems* provides a set of four evidence-based elements of high-quality care to all older adults known as the 4Ms.<sup>1</sup>
  - ▶ What Matters: Care is aligned with individual values and goals
  - ▶ Mobility: Move safely and maintain function
  - ▶ Medication: Treatment is necessary and non-redundant
  - ▶ Mentation: Prevent, identify, treat, and manage dementia, depression, and delirium

### Specific Considerations by Treatment Type

Surgery →

- Chronologic age is not the primary consideration for surgical risk<sup>2</sup>; all older adults undergoing surgery should undergo an assessment for components of frailty including comorbidities, cognition, mobility, functional status, and nutrition. For patients who are at high risk with multimorbidities and complex health conditions, consider multidisciplinary input with geriatric expertise.
- The [American College of Surgeons \(ACS\) Geriatric Surgery Verification \(GSV\) Program](#) provides a framework for hospitals to take an interdisciplinary approach to continuously optimize surgical care for older adults. The GSV Program includes 32 standards to improve surgical care for older adults with an emphasis on goals of care and shared decision-making, assessment of geriatric-specific vulnerabilities (eg, cognition, mobility), and interdisciplinary postoperative care.<sup>3</sup>
- The [ACS National Surgical Quality Improvement Program \(NSQIP\) Surgical Risk Calculator](#) includes both geriatric-specific predictors and geriatric-specific outcomes; the ACS NSQIP Surgical Risk Calculator can be a useful tool for sharing patient-specific predicted outcomes after surgery and facilitating a more informed discussion regarding risks of surgery.<sup>4</sup>
- Delirium is preventable and the most common postoperative complication in older adults; the American Geriatrics Society (AGS) practice guideline on postoperative delirium in older adults covers the topic areas of delirium risk factors, diagnosis and screening, prevention, medical evaluation, and pharmacologic treatment.<sup>5,6</sup> See [OAO-F 2 of 4](#).
- The surgical plan can be altered as necessary to consider non-surgical or less morbid options.

<sup>a</sup> Assessment of the patient's values and goals with regard to 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 ([OAO-2](#)).

[References](#)

Note: All recommendations are category 2A unless otherwise indicated.



## CONSIDERATIONS FOR OLDER ADULTS UNDERGOING CANCER-SPECIFIC TREATMENT<sup>a</sup>

Radiation  
therapy (RT)<sup>7-15</sup> →

- Improvements in RT techniques including intensity-modulated RT (IMRT), image-guided RT (IGRT), and stereotactic ablative radiotherapy (SABR) have improved the tolerability and therapeutic ratio of RT in older adults.
- Considerations of older patients undergoing RT should be informed by the benefits versus risks based on the anatomic site being radiated and the dose/fractionation chosen. Chronologic age by itself should not exclude patients from evaluation for curative RT.
- Use caution with concurrent chemoradiation therapy. Dose or sequence modification of chemotherapy or chemoradiation, additional supportive services, and more frequent monitoring may be necessary. See disease-specific [NCCN Guidelines for Treatment by Cancer Type](#).
- Hypofractionation and SABR may be considered to decrease the number of treatments, especially in patients who are frail and/or less mobile.
- Local ablative RT should be considered as an adjunct or alternative therapy in older adults.

Chemotherapy →

- Consider use of chemotherapy toxicity risk calculators where validated<sup>16,17</sup> to estimate toxicity and determine dose adjustments, additional supportive services, more frequent monitoring, and geriatric assessment as necessary.
  - ▶ Cancer and Aging Research Group (CARG) Chemo Toxicity Calculator ([http://www.mycarg.org/Chemo\\_Toxicity\\_Calculator](http://www.mycarg.org/Chemo_Toxicity_Calculator))
  - ▶ Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score (<https://www.mdcalc.com/calc/10425/chemotherapy-risk-assessment-scale-high-age-patients-crash-score>)<sup>18</sup>
  - ▶ Cancer and Aging Research Group-Breast Cancer (CARG-BC) score for older adults (for adjuvant/neoadjuvant therapy only) ([https://www.cancercalc.com/carg\\_bc.php](https://www.cancercalc.com/carg_bc.php))<sup>19</sup>

<sup>a</sup> Assessment of the patient's values and goals with regard to 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 ([OAO-2](#)).

[References](#)

Note: All recommendations are category 2A unless otherwise indicated.



## CONSIDERATIONS FOR OLDER ADULTS UNDERGOING CANCER-SPECIFIC TREATMENT<sup>a</sup>

Immunotherapy<sup>20-22</sup> →

- Overall, studies show that older patients have similar clinical benefit; however, closer and more aggressive follow-up may be needed related to toxicities.
- See disease-specific [NCCN Guidelines for Treatment by Cancer Type](#) and [NCCN Guidelines for the Management of Immunotherapy-Related Toxicities](#).

Targeted therapy<sup>23</sup> →

- Similar clinical benefit has been observed with these therapies in older patients compared to younger adults. However, side effects are not as well understood; thus, patients may require greater supervision with consideration of earlier and more aggressive management of side effects/toxicities.
- Oral targeted therapy should be closely monitored for adherence.
- See [NCCN Guidelines for Treatment by Cancer Type](#).

Cellular  
therapy/T-cell  
engagers<sup>24-27</sup> →

- Chimeric antigen receptor (CAR) T-cell therapy has been shown to be an effective therapeutic option for older adults with similar response rates as younger adults, and age should not be an absolute contraindication for the use of these therapies. However, older adults, especially those who are frail or unfit, may have a higher incidence of neurologic toxicities and require close monitoring ([NCCN Guidelines for the Management of Immunotherapy-Related Toxicities](#)).

<sup>a</sup> Assessment of the patient's values and goals with regard to 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 ([OAO-2](#)).

[References](#)

Note: All recommendations are category 2A unless otherwise indicated.



# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### MANAGEMENT OF COMMON SIDE EFFECTS IN OLDER ADULTS UNDERGOING CANCER-SPECIFIC TREATMENT<sup>a,j</sup>

- An older patient may have less reserve to manage toxicities. Complications may be more clinically significant and may require more intense surveillance.
- Consider that toxicities may have immediate or even long-term effects that are more significant.

GI-related (diarrhea, constipation, nausea/vomiting)	<ul style="list-style-type: none"> <li>• <a href="#">NCCN Guidelines for Antiemesis</a> and <a href="#">NCCN Guidelines for Palliative Care</a></li> </ul>
Mucositis	<ul style="list-style-type: none"> <li>• Early hospitalization is needed for patients with mucositis who also develop dysphagia/diarrhea.</li> <li>• Provide nutritional support. See <a href="#">NCCN Task Force: Prevention and Management of Mucositis in Cancer Care</a>.</li> </ul>
Bone marrow suppression	<ul style="list-style-type: none"> <li>• <a href="#">NCCN Guidelines for Hematopoietic Growth Factors</a></li> </ul>
Infection/immunosuppression	<ul style="list-style-type: none"> <li>• <a href="#">NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections</a></li> <li>• Assess if up to date on recommended vaccinations (<a href="#">NCCN Guidelines for Survivorship</a>)</li> </ul>
Neurotoxicity	<ul style="list-style-type: none"> <li>• Monitor hearing loss and avoid neurotoxic agents if significant hearing loss is present.</li> <li>• Monitor cerebellar function if treated with high-dose cytarabine.</li> <li>• Monitor for peripheral neuropathy.</li> <li>• Monitor for cognitive dysfunction (<a href="#">OAO-D 4 of 10</a>).</li> <li>• Consider polypharmacy (<a href="#">2023 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults</a>) (<a href="#">OAO-D 5 of 10</a>).</li> </ul>
Falls	<ul style="list-style-type: none"> <li>• Periodic assessment of history of falls, balance, and gait difficulties is recommended for all patients as fall risk may change over time<sup>28</sup> (<a href="#">OAO-E</a>).</li> <li>• The use of early and preventive use of durable medical equipment and in-home safety evaluations is recommended for patients at high risk for falls.</li> </ul>
Cardiac toxicity	<ul style="list-style-type: none"> <li>• Monitor for symptomatic or asymptomatic congestive heart failure (CHF).           <ul style="list-style-type: none"> <li>▶ Caution with use of anthracyclines; consider alternative treatment dosing schedule or treatment as appropriate per disease site (<a href="#">NCCN Guidelines for Treatment by Cancer Type</a>).</li> <li>▶ 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, SCARDIO-2, and SCARDIO-3 in the <a href="#">NCCN Guidelines for Survivorship</a>).<sup>29</sup></li> </ul> </li> </ul>

[Continued](#)

<sup>a</sup> Assessment of the patient's values and goals with regard to 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 ([OAO-2](#)).

<sup>j</sup> Assess for polypharmacy and use of non-prescribed agents as they can enhance these side effects ([2023 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults](#)) ([OAO-D 8 of 10](#)).

[References](#)

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# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### MANAGEMENT OF COMMON SIDE EFFECTS IN OLDER ADULTS UNDERGOING CANCER-SPECIFIC TREATMENT<sup>a,j</sup>

Renal toxicity	<ul style="list-style-type: none"> <li>Serum creatinine is not a good indicator of renal function in older adults. Calculation of estimated creatinine clearance is recommended to assess renal function and adjust dose to reduce systemic toxicity (<a href="#">OAO-D 2 of 10</a>).</li> </ul>
Insomnia ( <a href="#">OAO-G</a> )	<ul style="list-style-type: none"> <li>Benzodiazepines or other sedative-hypnotics should not be used as first-line treatment for insomnia in older adults<sup>30</sup>; non-pharmacologic methods such as cognitive behavioral therapy (CBT) and lifestyle modifications are preferred (see <a href="#">Sleep Disorders in NCCN Guidelines for Survivorship</a>).</li> </ul>
Immune-related adverse events (irAEs)	<ul style="list-style-type: none"> <li>High-dose steroids for the management of treatment-related toxicities must be used with caution in older patients as it may worsen other comorbidities or cognitive function.</li> <li><a href="#">NCCN Guidelines for the Management of Immunotherapy-Related Toxicities</a>.</li> </ul>

<sup>a</sup> Assessment of the patient's values and goals with regard to 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 ([OAO-2](#)).

<sup>j</sup> Assess for polypharmacy and use of non-prescribed agents as they can enhance these side effects ([2023 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults](#)) ([OAO-D 8 of 10](#)).

[References](#)

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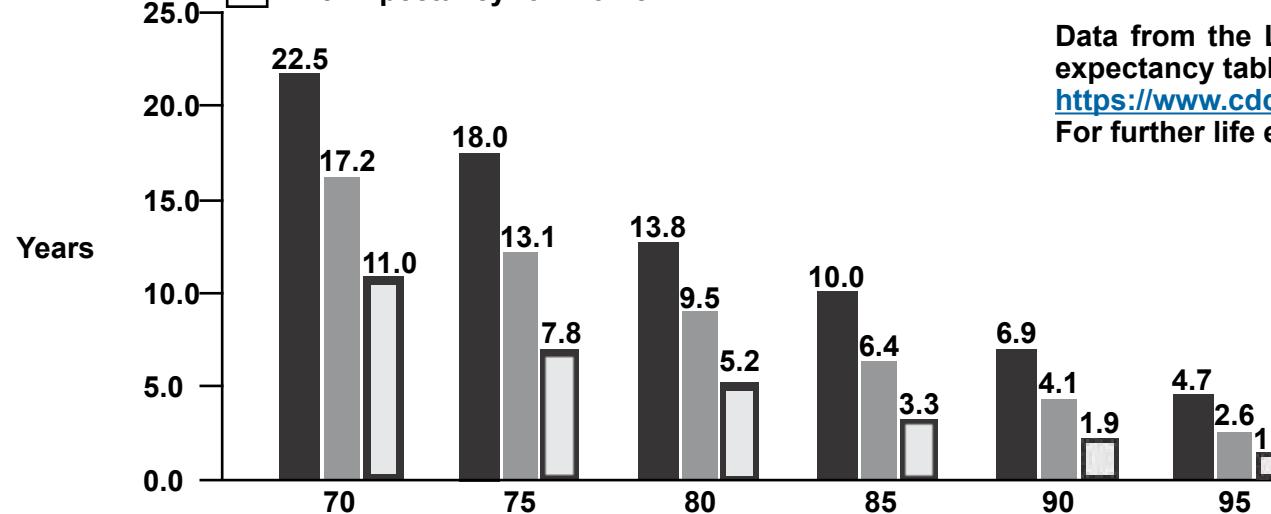
# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### LIFE EXPECTANCY OF GENERAL POPULATION

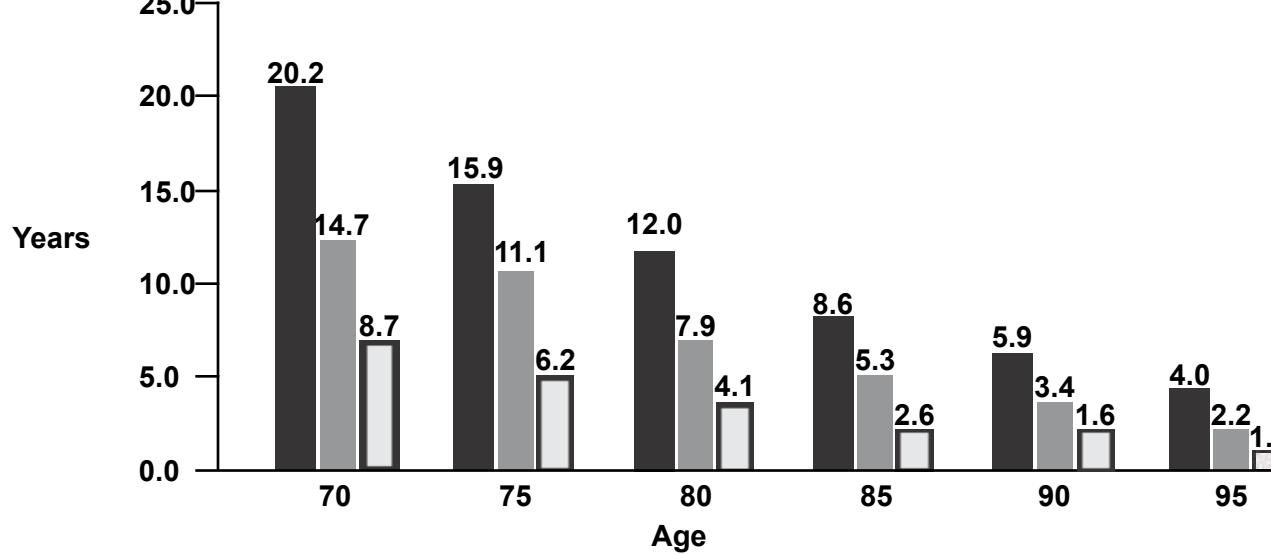
#### UPPER, MIDDLE, AND LOWER QUARTILES OF OVERALL AGE-SPECIFIC LIFE EXPECTANCY FOR WOMEN AND MEN

A Life Expectancy for Women



Data from the Life Tables of the United States, 2017. See the life expectancy tables in the National Vital Statistics Reports at [https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68\\_07-508.pdf](https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_07-508.pdf). For further life expectancy calculations, see [eprognosis.ucsf.edu](http://eprognosis.ucsf.edu).

B Life Expectancy for Men



Reprinted by permission from Kotwal AA, Walter LC. Cancer screening among older adults: A geriatrician's perspective on breast, cervical, colon, prostate, and lung cancer screening. Curr Oncol Rep 2020;22:108. ©Springer Nature.

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## GUIDANCE FOR THE OPTIMIZATION OF COMMUNICATION WITH OLDER ADULTS<sup>1</sup>

### Assess barriers to optimal communication:

- Assess for cognitive impairment ([OAO-F](#))
- Optimize vision – glasses if needed
- Optimize hearing – hearing aid, amplifying device (eg, pocket talker, provision of American Sign Language translators)
  - ▶ Ask the patient how best to communicate, and if hearing is better in one ear or the other
  - ▶ Speak toward the better ear and use a lower-pitched voice; minimize background noise
- Avoid jargon (eg, instead of “benign” use “not cancer” or instead of “metastasized” use “the cancer has spread”)
- Offer to include family and/or caregiver(s)

### Written materials (eg, after visit summaries):

- Offer written instructions after the appointment
- Write materials at the 5th grade level
- Use a large font (14 pt or larger)
- Use pictures that enhance the text
- Use black ink on white paper to optimize contrast

### Oral communication:

- Have the patient sit with their back to a wall (to help reflect sound)
- Face the patient when speaking, speak slowly and distinctly; don’t shout
- Rephrase rather than repeat
- Pause at the end of phrases or ideas
- For major concepts (prognosis, expected side effects, outcomes of treatment, and informed consent) always use the “teach back” (see [Teach-Back](#)) or “teach goal” method by querying the patient for understanding. Use questions such as: “I just gave you a lot of information and that can be confusing or a lot to absorb at once. Can you tell me in your own words what this chemotherapy will do for you/ how you will take your medicine, etc?”
- After each key concept, topic, or instruction, stop and ask, “What questions do you have?”
- Use a black board/white board or written materials to reinforce key concepts.
- Recognize the presence of, and avoid the use of, “elderspeak,” a form of communication used with older adults that is similar to “baby-talk” and may impact clinician-patient interactions and result in poor patient outcomes.<sup>2</sup>

<sup>1</sup> With permission from Reuben DB, Herr KA, Pacala JT, et al. Geriatrics At Your Fingertips: 2016, 18th Edition. New York: The American Geriatrics Society; 2016.

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## GUIDANCE FOR THE OPTIMIZATION OF COMMUNICATION WITH OLDER ADULTS

### Digital communication/Telehealth/Digital health<sup>3</sup>:

- Older adults appreciate choice in modality of health care (eg, in-person vs. telehealth).
- These could be supplemental to direct patient interaction, especially in rural areas with limited access.
- Ask about comfort level with different telehealth modalities: video, telephone, messaging/portal, and remote monitoring. Reassess periodically.
- Consider sensory impairments, connection quality, type of device, and patient's environment.
- Many self-reported or questionnaire-based screeners can be readily adapted to telehealth (eg, 30-second chair stand test).
- Some screeners may be generally reliable but not validated over telehealth (such as cognitive screeners with visual elements), so clinical judgment should be used in interpreting them and pursuing further evaluation.
- Benefits
  - ▶ Telehealth can lower appointment burden when a patient needs multiple appointments and allow for inclusion of supportive persons who are not physically present with the patient.
  - ▶ Video telehealth can provide insight into a patient's place of residence and can give the clinician additional insight into the social context.

<sup>3</sup> Powers BB, Van Zuilen RM, Schwartz AW, et al. Competencies for video telemedicine with older adult patients. J Am Geriatr Soc 2023;71:1283-1290.

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## IDENTIFICATION OF PATIENTS REQUIRING GERIATRIC ASSESSMENT<sup>a</sup>

Geriatric screening tools are used to identify older adults with cancer who would benefit from a geriatric assessment (GA) ([OAO-D 1 of 10](#)). All are self-reported and any of these tools can be used. Choose one.<sup>b</sup>

- [Abbreviated Comprehensive Geriatric Assessment \(aCGA\)](#)<sup>1,2</sup>
- [Barber Questionnaire](#)<sup>3</sup>
- [Fried Frailty Criteria](#)<sup>4,5</sup>
- [Geriatric 8 \(G-8\) Questionnaire](#)<sup>6,7</sup>
- [Groningen Frailty Index](#)<sup>2</sup>
- [Senior Adult Oncology Program \(SAOP\) 2](#)<sup>8,9</sup>
- [Triage Risk Screening Tool \(TRST\)](#)<sup>10</sup>
- [Vulnerable Elders Survey-13 \(VES-13\)](#)<sup>11,12,13</sup>
- [Self-Rated Health \(SRH\)](#)<sup>14</sup>

<sup>a</sup> For more information, see [Discussion](#).

<sup>b</sup> No evidence exists for superiority of these tools.

[References](#)

Note: All recommendations are category 2A unless otherwise indicated.

OAO-C  
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## IDENTIFICATION OF PATIENTS REQUIRING GERIATRIC ASSESSMENT

### REFERENCES

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OAO-C  
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## GERIATRIC ASSESSMENT (GA) AND INTERVENTIONS

GA is a multidisciplinary, in-depth evaluation that assesses the objective health of the older adult while evaluating multiple domains, which may affect cancer prognosis and treatment choices and tolerance. Appropriate use of geriatric screening tools and/or GA enables physicians to develop a coordinated plan for cancer treatment and to guide interventions tailored to the individual patient.<sup>1,2</sup>

### Reasons to Perform GA<sup>3,4</sup>

- GA can be helpful in re-assessing the patient's status throughout therapy.
- GA can reveal/detect reversible geriatric problems not found by routine oncology care.
- GA can predict risk of toxicity/adverse effects from cancer treatment.
- GA has important prognostic information that can be helpful in estimating life expectancy, which is of paramount importance when making treatment decisions.
- GA-guided care can reduce toxicity, and allows for targeted intervention, which can improve QOL and adherence to therapy.<sup>5,6</sup>
- GA can be helpful in improving communication of aging-related concerns.<sup>7</sup>

### Collaboration Between Geriatric Trained Clinician and Oncologist in the Care of an Older Patient with Cancer

Older adults may benefit from a referral to a geriatric trained clinician for assessment of vulnerability prior to cancer treatment, to develop a coordinated care plan with the oncologist and/or to manage geriatric syndromes that could jeopardize outcomes of cancer treatment. The geriatric trained clinician thus may be able to assist the oncologist in optimizing the management of the non-cancer aspects of the patient's care, which in turn may enable more effective delivery of direct cancer care. Consider consultation with a geriatric trained clinician for the following:

- Cognitive impairment
  - ▶ Dementia/delirium
  - ▶ Decision-making capacity evaluation
  - ▶ Life expectancy, advance directive/advance care planning, or guardianship ([NCCN Guidelines for Palliative Care](#))
- Functional or physical impairment, mobility issues, or disability
  - ▶ Falls evaluation and/or advice on falls prevention
  - ▶ Promote independent living or supportive living
- Multimorbidity including vision and hearing impairments
- Polypharmacy evaluation
- Presence of geriatric syndromes such as frailty, osteoporosis, depression, pressure ulcers, urinary incontinence, neglect or abuse, failure to thrive, or sarcopenia

[Continued](#)  
[References](#)

Note: All recommendations are category 2A unless otherwise indicated.

OAO-D  
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# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### GERIATRIC ASSESSMENT (GA)<sup>a</sup> AND INTERVENTIONS

- Patient's values and goals with regard to their cancer diagnosis can be used to inform treatment, decision planning, dose adjustments, schedule changes, etc. 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 <sup>b</sup> /Description	Additional Assessments/ Potential Interventions
Self-Reported Mobility and Function <a href="#">(OAO-D, 6 of 10)</a>	<p>Instrumental Activities of Daily Living (IADL)</p> <ul style="list-style-type: none"> <li>Measures ability to complete activities required to maintain independence ranging from making telephone calls to money management</li> <li>► <a href="#">OARS (Older Americans Resources and Services)</a></li> <li>► <a href="#">Lawton-Brody Instrumental Activities of Daily Living (IADL) Scale</a></li> </ul>	<ul style="list-style-type: none"> <li>Occupational therapy (OT) and physical therapy (PT) referral</li> <li>Physical medicine and rehabilitation referral</li> <li>Home safety evaluation health care</li> <li>Promote physical activity and exercise</li> <li>Evaluate medication use (consider orthostasis and overtreatment of hypertension [hypotension] and diabetes [hypoglycemia])</li> </ul>
	<p>Activities of Daily Living (ADL)</p> <ul style="list-style-type: none"> <li>Measures limitations in physical function activities, including bathing and dressing</li> <li>► <a href="#">Katz Index of Independence in Activities of Daily Living (ADL)</a></li> <li>► <a href="#">OARS</a></li> </ul>	
	<p>Falls (<a href="#">OAO-E</a>)</p> <ul style="list-style-type: none"> <li>Number of falls within the last 6 months</li> </ul>	
Objective Function and Mobility <a href="#">(OAO-E)</a>	<p><a href="#">Timed "Up and Go" (TUG)</a> Time it takes for individuals to stand up, walk 10 feet, return to chair, and sit back down</p>	<ul style="list-style-type: none"> <li>Referral to geriatric trained clinician or primary care physician</li> </ul>
	<p><a href="#">Timed 10-Meter Walk Test</a> Assesses functional mobility</p>	
	<p><a href="#">Short Physical Performance Battery (SPPB) Protocol and Score Sheet</a> Evaluation of lower extremity functioning</p>	
	<p><a href="#">Physical Performance Status</a> (Refer to Karnofsky or Eastern Cooperative Oncology Group [ECOG])</p>	

<sup>a</sup> Completion of the proposed GA will take an average of 20 minutes. Alternative tools that could be utilized are listed in the domain-specific section.

<sup>b</sup> All of these assessments can be performed in <5 minutes.

[Continued](#)

Note: All recommendations are category 2A unless otherwise indicated.



# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### GERIATRIC ASSESSMENT (GA)<sup>a</sup> AND INTERVENTIONS

Domain	Assessment Tools <sup>b</sup> /Description	Additional Assessments/Potential Interventions
Comorbidity <sup>c</sup>	<ul style="list-style-type: none"> <li>Assess the presence or absence of comorbidities           <ul style="list-style-type: none"> <li>▶ <a href="#">Charlson Comorbidity Index (CCI)</a></li> <li>▶ <a href="#">Cumulative Illness Rating Scale-Geriatric (CIRS-G)</a></li> <li>▶ <a href="#">OARS Questionnaire<sup>8,9</sup></a></li> </ul> </li> <li>Assess different categories of organ dysfunction and non-relapsed mortality risk           <ul style="list-style-type: none"> <li>▶ <a href="#">Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI)</a></li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Optimize each medical condition prior to therapy</li> <li>Coordinate with primary care physician and other specialists</li> <li>Evaluate life expectancy (<a href="#">Life Expectancy Table</a>)</li> <li>Consider comorbidities when deciding on treatment</li> </ul>
Social Functioning and Support ( <a href="#">OAO-D 6 of 10</a> )	<ul style="list-style-type: none"> <li>Measure the availability of social support, engagement in physical or social activities, and loneliness/social isolation           <ul style="list-style-type: none"> <li>▶ <a href="#">MOS Social Support Survey</a></li> <li>▶ <a href="#">UCLA 3-Item Loneliness Scale</a></li> </ul> </li> <li>Evaluate the self-reported availability of emotional/informational social support           <ul style="list-style-type: none"> <li>▶ <a href="#">RAND Health Care Social Support Survey Instrument: Emotional/Informational Subscale</a></li> </ul> </li> <li>Evaluate the self-reported availability of tangible physical social support           <ul style="list-style-type: none"> <li>▶ <a href="#">RAND Health Care Social Support Survey: Tangible Subscale</a></li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Refer to social work for:           <ul style="list-style-type: none"> <li>▶ Transportation assistance</li> <li>▶ Financial toxicity<sup>10</sup></li> <li>▶ Home health care</li> <li>▶ Support groups</li> <li>▶ Food/housing insecurity</li> <li>▶ Caregiver status assessment (<a href="#">OAO-K 1 of 3</a>)</li> <li>▶ Elder abuse screening; ask the patient, "Do you feel safe at home?"</li> <li>▶ Language barrier and need for interpreter support</li> <li>▶ Medication assistance programs, change in level of care, facilitations to assisted living, respite care, skilled nursing facilities, arrangement to local agencies on aging and community resources</li> </ul> </li> <li>Home safety evaluation/referral for medical alert devices</li> <li>Refer to psychiatry/psychology</li> <li>Spiritual care</li> </ul>

<sup>a</sup> Completion of the proposed GA will take an average of 20 minutes. Alternative tools that could be utilized are listed in the domain-specific section.

<sup>b</sup> All of these assessments can be performed in <5 minutes.

<sup>c</sup> Comorbidity is being used instead of multimorbidity, since cancer is the predominant disease.

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Note: All recommendations are category 2A unless otherwise indicated.

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# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### GERIATRIC ASSESSMENT (GA)<sup>a</sup> AND INTERVENTIONS

Domain	Assessment Tools <sup>b</sup> /Description	Additional Assessments/Potential Interventions
Cognition <a href="#">(OAO-F)</a>	<ul style="list-style-type: none"> <li>Evaluate the level of cognitive impairment, if any           <ul style="list-style-type: none"> <li>▶ <a href="#">Mini-Cog</a></li> <li>▶ <a href="#">Mini-Mental State Examination (MMSE)<sup>d,e</sup></a></li> <li>▶ <a href="#">Blessed Orientation Memory Concentration Test (BOMC)</a></li> <li>▶ <a href="#">Montreal Cognitive Assessment (MoCA)<sup>e</sup></a></li> <li>▶ <a href="#">Saint Louis University Mental Status Exam (SLUMS)</a></li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Involve family/caregiver</li> <li>• Assess/minimize potentially inappropriate medications (<a href="#">OAO-H</a>)</li> <li>• Prevent delirium (<a href="#">OAO-F 4 of 4</a>)</li> <li>• Assess capacity and ability to consent to treatment (<a href="#">OAO-2</a>)</li> <li>• Identify health care proxy/collaborative decision maker</li> <li>• Provide written summary</li> <li>• Provide cognitive testing/referral to neuropsychologist/geriatric trained clinician</li> <li>• Consider referral for cognitive rehabilitation</li> </ul>
Psychological	<ul style="list-style-type: none"> <li>Evaluate for the risk for depression           <ul style="list-style-type: none"> <li>▶ <a href="#">Geriatric Depression Scale-4 (GDS-4)</a></li> <li>▶ <a href="#">Patient Health Questionnaire (PHQ-2 and PHQ-9)<sup>11</sup></a></li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Provide complementary (non-pharmacologic) modalities such as guided imagery, meditation, relaxation, acupuncture, etc.</li> <li>• Refer to integrative medicine</li> <li>• Provide counseling by a qualified professional</li> <li>• Refer to psychiatry/psychology</li> <li>• Start medication to treat anxiety/depression</li> <li>• Provide support programs</li> <li>• Provide spiritual care</li> <li>• Assess for substance and alcohol use disorder</li> </ul>
	<ul style="list-style-type: none"> <li>Evaluates the level of depression and anxiety experienced in the last month           <ul style="list-style-type: none"> <li>▶ <a href="#">Mental Health Inventory Survey (MHI-17)</a></li> </ul> </li> </ul>	
	<ul style="list-style-type: none"> <li>Evaluates the level of distress           <ul style="list-style-type: none"> <li>▶ <a href="#">Distress thermometer (NCCN Guidelines for Distress Management)</a></li> </ul> </li> </ul>	

<sup>a</sup> Completion of the proposed GA will take an average of 20 minutes. Alternative tools that could be utilized are listed in the domain-specific section.

<sup>b</sup> All of these assessments can be performed in <5 minutes.

<sup>d</sup> Folstein MF, Folstein SE, McHugh PR. "Mini mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.

<sup>e</sup> Licensing is required for using these tools.

[Continued](#)  
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Note: All recommendations are category 2A unless otherwise indicated.

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# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### GERIATRIC ASSESSMENT (GA)<sup>a</sup> AND INTERVENTIONS

Domain	Assessment Tools <sup>b</sup> /Description	Additional Assessments/Potential Interventions
<b>Nutrition<sup>4,12,13</sup> (OAO-D, 7 of 10)</b>	<p><b>Body Mass Index (BMI)</b> Weight (kg)/Height (m<sup>2</sup>)</p> <p>Percent unintentional weight loss in last 6 months</p> <p><b>Mini-Nutritional Assessment (MNA)</b> Validated self-reported tool that can identify older adults who are malnourished or at risk for malnutrition</p>	<ul style="list-style-type: none"> <li>• Nutrition consult</li> <li>• Make specific dietary recommendations</li> <li>• Oral care</li> <li>• Supplemental nutrition</li> <li>• OT for assistive devices</li> <li>• Speech therapy and swallowing assessment</li> <li>• Oral and dental evaluation for dentures</li> <li>• Evaluation for appetite stimulants-nausea control/calorie/protein fluid recommendations/food insecurity (eg, local food banks, Meals on Wheels), treatment with dietary supplements</li> <li>• Provide nutrition education for management of nutrition impact symptoms</li> <li>• <a href="#">Guide to Nutritional Intervention from NCI Nutrition in Cancer Care (PDQ)</a></li> </ul>
<b>Medications<sup>14-17</sup> (OAO-D, 8 of 10)</b>	<p><b>Medications</b> Prescription and non-prescription medications or substances</p> <p><a href="#">2023 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults</a></p> <p><b>Screening Tool of Older Persons' Prescriptions (STOPP)</b></p> <p><b>Screening Tool to Alert to Right Treatment (START) criteria</b></p> <p><b>Medication Appropriateness Index (MAI)</b></p>	<ul style="list-style-type: none"> <li>• Medication reconciliation with patient and other care providers</li> <li>• Evaluate for opioid and substance abuse</li> <li>• Discontinue inappropriate or unnecessary medications</li> <li>• Evaluate for drug-drug and drug-disease interactions</li> <li>• Evaluate for the use of supplements and herbal therapies</li> </ul>

<sup>a</sup> Completion of the proposed GA will take an average of 20 minutes. Alternative tools that could be utilized are listed in the domain-specific section.

<sup>b</sup> All of these assessments can be performed in <5 minutes.

Note: All recommendations are category 2A unless otherwise indicated.

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## GERIATRIC ASSESSMENT (GA) AND INTERVENTIONS

### Functional Status

- ADL - Self-feeding, dressing, continence, grooming, transferring, using the bathroom
- IADL - Using transportation, managing money, taking medications, shopping, preparing meals, doing laundry, doing housework, using the telephone
- Physical Performance Status (refer to Karnofsky or ECOG)
- Visual function and/or hearing impairment
- Falls and/or unstable gait
  - ▶ Falls are more common in older adults with cancer than those without cancer
  - ▶ Factors that have been prospectively associated with increased risk of subsequent falls in older adults with cancer include: prior falls, benzodiazepine use, cancer pain, and neurotoxic chemotherapy
  - ▶ In patients who are at risk, such as those who have experienced a fall in the last 6 months or if the patient is “afraid of falling,” consider the following evaluations:
    - ◊ Assessment of gait by evaluating gait speed<sup>18</sup> or using the TUG test ([OAO-E](#))
    - ◊ Exercise promotion including PT or OT evaluation, as needed
    - ◊ Checking vitamin D levels and supplementing vitamin D if low and assess bone mineral density (BMD)<sup>19</sup>
    - ◊ Referral to geriatrics or primary care physician
    - ◊ Home safety evaluation and home modifications as indicated
    - ◊ Medications that put patients at risk for adverse outcomes [[Medications Commonly Used for Supportive Care that Are of Concern in Older Patients \(OAO-H\)](#)]

### Socioeconomic Considerations

Evaluate/assess for the following (refer to social work as appropriate):

- Language barriers and need for interpreter support
- Cultural considerations
- Living conditions
  - ▶ Family/caregiver or social support
  - ▶ Income
  - ▶ Elder abuse
  - ▶ Safety at home
- Loneliness and isolation ([UCLA 3-Item Loneliness Scale](#))
- Transportation barriers/access problems
- Food insecurity
- Financial toxicity (eg, underinsurance and/or high out-of-pocket costs)<sup>10</sup>

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Note: All recommendations are category 2A unless otherwise indicated.

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## GERIATRIC ASSESSMENT (GA) AND INTERVENTIONS

### Nutritional Status

Patients with cancer are at risk for severe malnutrition that is underdiagnosed.<sup>20</sup>

- Poor nutritional status is associated with increased mortality and poor chemotherapy tolerance.
- Malnutrition among hospitalized patients with cancer is associated with increased length of stay.<sup>20</sup>

► Practical consideration to guide further nutritional assessment of patients at risk for malnutrition includes:

- ◊ Unintentional weight loss of >5% over 6 months.<sup>21</sup> As per ASPEN guidelines, unintentional weight loss is considered: ≥5% in 1 month, ≥10% in 6 months.<sup>22</sup>
- ◊ BMI of ≤22
- ◊ Weighing <80% of ideal body weight<sup>23</sup>
- ◊ Practical suggestions for evaluation of and treatment for optimizing nutrition among patients with cancer:
  - [Guide to Nutritional Intervention from NCI Nutrition in Cancer Care \(PDQ\)](#)
  - [MNA](#)
- ◊ Referral to speech and language pathologist to assess for swallowing issues

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[References](#)

Note: All recommendations are category 2A unless otherwise indicated.

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### GERIATRIC ASSESSMENT (GA) AND INTERVENTIONS

#### MEDICATIONS

**Medication Reconciliation<sup>f</sup>:** Reconcile medications at every visit, including prescription and over-the-counter medications, vitamins, and supplements.

**Medication Review<sup>g,h,14-17,24-26</sup>:** Medication review is indicated with transitions of care, any initiation or change in oncologic treatment, change in comorbid disease management, or change in clinical condition.

- Does every medication match a known medical problem or chronic condition? Any deficiencies or duplications?
- Are the dosages appropriate for each medication for the patient's age, renal function, or liver function?
- Are there potential drug-drug or drug-disease interactions<sup>i</sup> or other adverse effects of the medication?
- Could a medication-related problem be responsible for current complaints or presenting problems?
- Can the medication regimen be simplified? Consider deprescribing as appropriate.
- Are there any less expensive alternative medications that are of equal utility?

#### Potential Inappropriate Prescribing

- Carefully review indications, duration of therapy, and dosage when using these medications or classes of medications that are not recommended for older adults. See [Medications Commonly Used for Supportive Care that Are of Concern in Older Patients \(OAO-H\)](#).
- Are there any high-risk/low-benefit or inappropriate medications?
- Use an evidenced-base instrument for the determination of a medication appropriateness: Beers Criteria,<sup>27</sup> STOPP,<sup>28</sup> START criteria,<sup>29</sup> MAI<sup>30</sup>

#### Medication Adherence

- Always assess risk of non-adherence, especially when considering a treatment regimen that will include an oral agent.<sup>31</sup>

<sup>f</sup> Medication reconciliation refers to the process of developing an accurate list of medications a patient is taking.

<sup>g</sup> Medication review refers to the process of providing a structural, critical evaluation of a patient's medication list in order to optimize care and avoid harm.

<sup>h</sup> Memorial Sloan Kettering Cancer Center Search About Herbs. Available at: <https://www.mskcc.org/cancer-care/diagnosis-treatment/symptom-management/integrative-medicine/herbs/search>.

<sup>i</sup> <https://medicine.iu.edu/internal-medicine/specialties/clinical-pharmacology/drug-interaction-flockhart-table/app>

<sup>j</sup> Confirm ability to read and comprehend written instructions (eg, vision, literacy).

#### References

Note: All recommendations are category 2A unless otherwise indicated.

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## Older Adult Oncology

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### GERIATRIC ASSESSMENT (GA) AND INTERVENTIONS

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Note: All recommendations are category 2A unless otherwise indicated.

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## GERIATRIC ASSESSMENT (GA) AND INTERVENTIONS

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Note: All recommendations are category 2A unless otherwise indicated.

**FALLS ASSESSMENT AND INTERVENTIONS**

Assessment of gait by evaluating gait speed or using the TUG test<sup>1,2,3</sup> ([OAO-D, 2 of 10](#))

- The TUG test is calculated as the time in seconds it takes a patient to stand up from a chair (without using their arms), walk 10 feet straight ahead, turn back, and return to the chair and sit down. The patient may use an assistive device, such as a cane or walker, but may not have assistance from another person.
- A normal TUG test score is <13 seconds. For patients with above-normal TUG test scores, consider comprehensive evaluation as indicated below.

ASSESSMENT	INTERVENTIONS
Assess proximal muscle strength	<ul style="list-style-type: none"> <li>• Diagnose and treat underlying causes</li> <li>• Consider PT evaluation</li> </ul>
Mobility aids assessment	<ul style="list-style-type: none"> <li>• Assess for type, condition, usage technique, and fit of mobility aid</li> <li>• Consider referral for OT/PT evaluation</li> <li>• Physical medicine and rehabilitation referral</li> </ul>
Check orthostatic blood pressure	<ul style="list-style-type: none"> <li>• Diagnose and treat underlying causes</li> <li>• Review medications</li> <li>• Address salt intake, adequate hydration, and compensatory strategies (eg, elevating head of bed, rising slowly, using pressure stockings or an abdominal binder<sup>4</sup>)</li> </ul>
Ask about vision changes	<ul style="list-style-type: none"> <li>• Diagnose and treat underlying cause of vision changes</li> <li>• Consider referral to ophthalmologist</li> <li>• Consider neurologic evaluation</li> <li>• OT referral</li> </ul>
Assess for neurologic changes	<ul style="list-style-type: none"> <li>• Evaluate if cancer or cancer treatment-related and modify treatment if possible</li> <li>• Consider neurologic evaluation</li> </ul>
Review medications	<ul style="list-style-type: none"> <li>• See "Medications" (<a href="#">OAO-D, 8 of 10</a>)</li> </ul>
Environmental hazards	<ul style="list-style-type: none"> <li>• Consider home safety evaluation</li> <li>• Educate patients to reduce risk (<a href="https://www.cdc.gov/steady/pdf/STEADI-Brochure-CheckForSafety-508.pdf">https://www.cdc.gov/steady/pdf/STEADI-Brochure-CheckForSafety-508.pdf</a>)</li> </ul>
Footwear assessment	<ul style="list-style-type: none"> <li>• Assess type, condition, and fit of shoes</li> <li>• Perform foot examination</li> <li>• Consider referral to podiatrist</li> </ul>

<sup>3</sup> Vande Walle N, et al. BMC Geriatr 2014;14:135.

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**NCCN Guidelines Version 1.2025**  
**Older Adult Oncology****ASSESSMENT OF COGNITIVE FUNCTION<sup>1,2</sup>**

When to Assess for Cognitive Function	Recommendations
Would impaired cognitive function affect the planning or delivery of care? (eg, impact life expectancy or risk/benefit, impact adherence to treatment plan)	No (to all) → Reassess periodically or when considering treatment plan changes
Is the medical team concerned about decision-making capacity? See <a href="#">OAO-2</a>	
Does the patient have a history of recent delirium or late onset of depression?	
Does the medical team suspect impaired cognitive function?	
Has the patient or patient's family/caregiver suggested that the patient has impaired cognitive function?	Yes (to any) → Consult with a clinician experienced in cognitive evaluation (ie, geriatrician, neurologist, geriatric psychiatrist, neuropsychologist, occupational therapist) OR Initiate the evaluation yourself ( <a href="#">OAO-F, 2 of 4</a> )

<sup>1</sup> Cordell CB, Borson S, Boustani M, et al; Medicare Detection of Cognitive Impairment Workgroup. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting. *Alzheimers Dement* 2013;9:141-150.

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Note: All recommendations are category 2A unless otherwise indicated.

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### ASSESSMENT OF COGNITIVE FUNCTION<sup>1,2,3</sup>

	Mild Cognitive Impairment	Dementia	Delirium
Definition	An intermediate state between normal cognition and dementia characterized by: <b>Subjective memory impairment</b> <b>Preserved general cognitive function</b> <b>Intact ability to perform daily functions</b>	A progressive condition characterized by: <b>Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains</b> <b>Interference with ability to perform daily functions (ADL/IADL, <a href="#">OAO-D, 2 of 10</a>)</b>	<b>Disturbance in attention and awareness:</b> <b>Onset over a short period of time (usually hours to days)</b> <b>Fluctuation during the course of the day</b> See <a href="#">OAO-F 4 of 4</a> for risk factors and strategies for the prevention of delirium
Distinguishing Features	<b>Subjective memory complaints and awareness of memory changes</b> <b>Preserved function</b>	<b>Progressive (not sudden) loss of multiple cognitive abilities</b> <b>Affects the ability to function independently</b>	<b>Acute onset</b> <b>Waxing and waning attention</b> <b>Associated with physiologic disturbances</b> <b>Increased in postoperative setting<sup>4</sup></b>
Differential Diagnosis (confounding factors)	<b>Central nervous system (CNS) metastases</b> <b>Psychiatric disease (depression, anxiety, apathy)</b> <b>Endocrine dysfunction (thyroid)</b> <b>Metabolic causes (B12 deficiency)</b> <b>Drug dependency (including alcohol)</b> <b>Medication related</b> <b>Sleep disturbance</b> <b>Common geriatric conditions (pain, infection, constipation)</b>		

<sup>1</sup> Cordell CB, Borson S, Boustani M, et al; Medicare Detection of Cognitive Impairment Workgroup. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness visit in a primary care setting. *Alzheimers Dement* 2013;9:141-150.

<sup>2</sup> Simpson JR. DSM-5 and neurocognitive disorders. *J Am Acad Psychiatry Law* 2014;42:159-164.

<sup>3</sup> If you have concerns about decision-making capacity, see ([OAO-2](#)).

<sup>4</sup> American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults. American Geriatrics Society abstracted clinical practice guideline for postoperative delirium in older adults. *J Am Geriatr Soc* 2015;63:142-150.

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Note: All recommendations are category 2A unless otherwise indicated.

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# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### ASSESSMENT OF COGNITIVE FUNCTION<sup>1,2,3</sup>

	Mild Cognitive Impairment	Dementia	Delirium
<b>Screening Tool</b>	Cognitive ( <a href="#">Mini-Cog</a> ), MMSE, <sup>5,6</sup> MoCA, <sup>6</sup> <a href="#">SLUMS</a> , and functional (ADL/ IADL, <a href="#">OAO-D, 2 of 10</a> ) assessment	Cognitive ( <a href="#">Mini-Cog</a> ), MMSE, <sup>5,6</sup> MoCA, <sup>6</sup> <a href="#">SLUMS</a> , and functional (ADL/ IADL, <a href="#">OAO-D, 2 of 10</a> ) assessment	<a href="#">Confusion Assessment Method (CAM)</a> <sup>7</sup>
<b>Further Evaluation</b>	Reassess periodically and with major changes in condition or when considering changes to treatment plan If screening is abnormal, consult with a clinician experienced in cognitive evaluation	Consult with a clinician experienced in cognitive evaluation and treatment Neuropsychological testing may be indicated Evaluation: B12, thyroid-stimulating hormone (TSH), brain imaging See DIS-7 and DIS-8 in the <a href="#">NCCN Guidelines for Distress Management</a>	Evaluate and treat all potential causes of delirium If screening is abnormal consult with a clinician experienced in cognitive evaluation See DIS-7 and DIS-8 in the <a href="#">NCCN Guidelines for Distress Management</a>
<b>Communication</b>		Refer to guidance from the Alzheimer's Association: <a href="https://www.alz.org/help-support/caregiving/daily-care/communications">https://www.alz.org/help-support/caregiving/daily-care/communications</a>	

<sup>1</sup> Cordell CB, Borson S, Boustani M, et al; Medicare Detection of Cognitive Impairment Workgroup. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness visit in a primary care setting. Alzheimers Dement 2013;9:141-150.

<sup>2</sup> Simpson JR. DSM-5 and neurocognitive disorders. J Am Acad Psychiatry Law 2014;42:159-164.

<sup>3</sup> If you have concerns about decision-making capacity, see ([OAO-2](#)).

<sup>5</sup> Folstein MF, Folstein SE, McHugh PR. "Mini mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.

<sup>6</sup> Licensing is required for using these tools.

<sup>7</sup> Confusion Assessment Method. © 1988, 2003, Hospital Elder Life Program. All rights reserved. Adapted from: Inouye SK, et al. Ann Intern Med 1990;113:941-948.

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Note: All recommendations are category 2A unless otherwise indicated.

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# NCCN Guidelines Version 1.2025

## Older Adult Oncology

### ASSESSMENT OF COGNITIVE FUNCTION<sup>1,2,3</sup>

Risk Factors for the Development of Delirium in Older Patients With Cancer<sup>8,9</sup>

PREDISPOSING FACTORS	PRECIPITATING FACTORS	CANCER-RELATED FACTORS
Advanced Age	New psychoactive drugs	Primary CNS tumors
Preexisting cognitive impairment	Dehydration and/or electrolyte disturbance	Secondary CNS tumors: Brain or meningeal metastasis
Previous history of delirium	Immobility	Para-neoplastic neurological syndromes
Polypharmacy	Constipation/fecal impaction	Toxicities from anticancer treatment: radiation to the brain, chemotherapy, immunotherapy
Sensory impairment (vision, hearing)	Urinary retention/bladder catheters	Toxicities from chemotherapy support (eg, antihistamines, steroids, antiemetics, anxiolytics, opioids)
Functional dependency	Malnutrition	
History of alcohol use disorder	Pain	
Multiple comorbid conditions	Use of physical restraints	
Malnutrition	Severe illness (eg, sepsis, stroke)	

### Strategies for Prevention of Delirium

- The strongest evidence supports the reduction of the common risk factors such as polypharmacy, sleep deprivation, immobility, visual and hearing impairment, malnutrition, and dehydration.
- Reduce psychoactive medications as a first step wherever possible.
- Reserve pharmacologic interventions for patients with severe agitation, which will result in interruption of essential medical therapies or poses a danger for self-injury; or for those with distressing psychotic symptoms (eg, hallucinations, delusions).
- Patients with one or more of these risk factors should receive non-pharmacologic interventions to address them.

### Non-pharmacologic Interventions for the Treatment of Delirium

- Non-pharmacologic interventions are the cornerstone of delirium treatment.
- These interventions include:
  - Identification and elimination of factors contributing to delirium
  - Frequent reorientation
  - Involvement of family members
  - Symptom management; treat dehydration and constipation
  - Thorough medication review, promotion of mobility and sleep hygiene

<sup>1</sup> Cordell CB, Borson S, Boustani M, et al; Medicare Detection of Cognitive Impairment Workgroup. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness visit in a primary care setting. Alzheimers Dement 2013;9:141-150.

<sup>2</sup> Simpson JR. DSM-5 and neurocognitive disorders. J Am Acad Psychiatry Law 2014;42:159-164.

<sup>3</sup> If you have concerns about decision-making capacity, see [\(OAO-2\)](#).

<sup>8</sup> Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet 2014;383:911-922.

<sup>9</sup> Bush SH, Lawlor PG, Ryan K, et al. Delirium in adult cancer patients: ESMO Clinical Practice Guidelines. Ann Oncol 2018;29:iv143-iv165.

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## INSOMNIA

- The AGS provides recommendations for the diagnosis, evaluation, and management of insomnia.
- Benzodiazepines or other sedative-hypnotics should not be used as first-line treatment for insomnia in older adults.<sup>a</sup>
- Non-pharmacologic methods such as sleep hygiene, CBT, and lifestyle modifications are preferred.
- Patient should be cautioned that most over-the-counter sleep medications contain antihistamines and should not be used in older adults.
- If pharmacologic therapy is to be utilized, it is recommended for short-term use only with the lowest dose that is effective. The risks and benefits of the therapy should be discussed.<sup>b</sup>
- Please note that if zolpidem is considered, the U.S. Food and Drug Administration (FDA) has advised that the recommended dose of zolpidem for females should be lowered from 10 mg to 5 mg for immediate-release products and from 12.5 mg to 6.25 mg for extended-release products.<sup>c</sup>
- Patient information regarding optimizing sleep is available through the National Institute on Aging.<sup>d</sup>
- See sleep medication recommendations ([OAO-H, 2 of 7](#)).

<sup>a</sup> See American Geriatrics Society: Ten Things Clinicians and Patients Should Question (<http://www.choosingwisely.org/doctor-patient-lists/american-geriatrics-society>).

<sup>b</sup> See AGS Geriatrics Evaluation & Management Tools (GEMS): <http://www.americageriatrics.org>.

<sup>c</sup> See <https://www.fda.gov/drugs/drugsafety/ucm334041.htm>.

<sup>d</sup> See <http://www.nia.nih.gov/health/publication/good-nights-sleep>.

**Note:** All recommendations are category 2A unless otherwise indicated.



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### MEDICATIONS COMMONLY USED FOR SUPPORTIVE CARE THAT ARE OF CONCERN IN OLDER PATIENTS

Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
<b>Corticosteroids (oral)<sup>1,2,3,4,5,6</sup>:</b> • hydrocortisone • methylprednisolone • prednisone • prednisolone • dexamethasone	<ul style="list-style-type: none"> <li>Weight gain</li> <li>Muscle weakness</li> <li>Agitation</li> <li>Hyperglycemia/Diabetes</li> <li>Cushing syndrome</li> <li>Osteoporosis</li> <li>Delirium</li> <li>Insomnia</li> <li>Increased risk of gastrointestinal (GI) bleed, infection, fracture, thromboembolism</li> </ul>	<ul style="list-style-type: none"> <li>When used for supportive care, carefully consider the dose and duration of therapy.</li> <li>Use the lowest possible dose ideally for short-term therapy (1–3 weeks).</li> <li>Short-term use as an adjuvant for pain or antiemetic, for spinal cord compression, increased intracranial pressure, and bowel obstruction is appropriate (when benefit outweighs risk).</li> <li>For management of irAE, use the lowest possible effective dose.</li> </ul>	<p>When risk outweighs benefit:</p> <ul style="list-style-type: none"> <li>For pain, consider other adjuvant pain medications (eg, gabapentin,<sup>a</sup> serotonin-norepinephrine reuptake inhibitor [SNRI] antidepressants,<sup>b</sup> lamotrigine,<sup>a</sup> topical lidocaine, as indicated by type of pain and response).</li> <li>For nausea, consider alternative antiemetics (eg, serotonin antagonists, aprepitant).</li> </ul>

<sup>a</sup> Unlabeled use.<sup>b</sup> Not all medications in this class are labeled for this use.[Continued](#)  
[References](#)**Note:** All recommendations are category 2A unless otherwise indicated.



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## Older Adult Oncology

### MEDICATIONS COMMONLY USED FOR SUPPORTIVE CARE THAT ARE OF CONCERN IN OLDER PATIENTS

Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
<b>Benzodiazepines<sup>4,5,7,8</sup>:</b> • alprazolam • estazolam • lorazepam • oxazepam • temazepam • triazolam • clorazepate • chlordiazepoxide • clonazepam • diazepam • flurazepam • quazepam	<ul style="list-style-type: none"> <li>Older adults have increased sensitivity and slower metabolism of benzodiazepines</li> <li>Increased risk for falls, cognitive impairment, delirium</li> </ul>	<ul style="list-style-type: none"> <li>Avoid for treatment of insomnia,<sup>9</sup> agitation, or delirium.</li> <li>Potentially appropriate for seizures, rapid eye movement sleep disorders, benzodiazepine withdrawal, alcohol withdrawal, severe generalized anxiety disorders, and end-of-life care.</li> <li>Reduce dose and/or lengthen the dosing interval when using for supportive care during chemotherapy administration.</li> <li>Avoid abrupt discontinuation or quick taper after chronic use in order to prevent significant withdrawal symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>For anxiety, consider buspirone, selective serotonin reuptake inhibitors (SSRIs),<sup>a</sup> or SNRIs.<sup>a</sup></li> <li>For sleep, use sleep hygiene education, sleep restriction or sleep compression,<sup>c</sup> or CBT. See <a href="#">Insomnia (OAO-G)</a> and <a href="#">NCCN Guidelines for Survivorship</a>.</li> <li>For nausea, consider an alternative agent. See <a href="#">NCCN Guidelines for Antiemesis</a>.</li> </ul>
<b>Non-benzodiazepine sedative hypnotics<sup>7,8</sup>:</b> • zolpidem • eszopiclone • zaleplon	<ul style="list-style-type: none"> <li>Similar adverse effects to benzodiazepines with minimal improvement in sleep latency and duration</li> <li>Delirium</li> <li>Falls/fractures</li> </ul>	<ul style="list-style-type: none"> <li>Use no more than 2 to 3 days per week for up to 90 days.</li> <li>Avoid chronic use.</li> <li>If zolpidem is used, the dose in females should not exceed 5 mg.</li> </ul>	<ul style="list-style-type: none"> <li>Use sleep hygiene education, sleep restriction or compression, or CBT. In the right setting, if pharmacologic therapy is deemed necessary, agents such as trazodone,<sup>a</sup> mirtazapine,<sup>a</sup> melatonin,<sup>a</sup> ramelteon, or other medications could be considered, keeping in mind the risks and benefits of each individual therapy. See <a href="#">Insomnia (OAO-G)</a> and <a href="#">Sleep Disorders in the NCCN Guidelines for Survivorship</a>.</li> </ul>

<sup>a</sup> Unlabeled use.<sup>c</sup> Sleep compression is an incremental decrease of time spent in bed.

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## Older Adult Oncology

### MEDICATIONS COMMONLY USED FOR SUPPORTIVE CARE THAT ARE OF CONCERN IN OLDER PATIENTS

Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
<b>First-generation antihistamines<sup>4,5,7,8</sup>:</b> • diphenhydramine • hydroxyzine • promethazine • brompheniramine • carbinoxamine • clemastine • cyproheptadine • dexbrompheniramine • dexchlorpheniramine • doxylamine • triprolidine	<ul style="list-style-type: none"> <li>Anticholinergic toxicities</li> <li>Confusion</li> <li>Cognitive impairment</li> <li>Delirium</li> <li>Dry mouth</li> <li>Constipation</li> <li>Urinary retention</li> <li>Clearance is reduced</li> </ul>	<ul style="list-style-type: none"> <li>Use only for supportive care when convincing benefit exists.</li> <li>Appropriate for acute treatment of severe allergic reactions.</li> </ul>	<ul style="list-style-type: none"> <li>Consider second-generation antihistamines (ie, cetirizine, desloratadine, loratadine, fexofenadine, levocetirizine), intranasal antihistamines, intranasal anticholinergics, or leukotriene inhibitors.</li> <li>For sleep, use sleep hygiene education, sleep restriction or sleep compression, or CBT. See <a href="#">Insomnia (OAO-G)</a> and <a href="#">NCCN Guidelines for Survivorship</a>.</li> </ul>
<b>Antiemetic, prokinetic<sup>6,7,8</sup>:</b> • metoclopramide • NK-1 antagonists ▶ Aprepitant ▶ Fosaprepitant ▶ Rolapitant <b>Phenothiazine antiemetics<sup>7</sup>:</b> • prochlorperazine	<ul style="list-style-type: none"> <li>May cause extrapyramidal effects</li> <li>Greater risk of falls in older patients</li> <li>Can worsen parkinsonian symptoms</li> </ul>	<ul style="list-style-type: none"> <li>Avoid metoclopramide, unless use is for patients with gastroparesis.</li> <li>If benefit outweighs risk, use the lowest metoclopramide dose possible, and avoid exceeding 5 mg.</li> <li>Really dose adjust metoclopramide.</li> </ul>	<ul style="list-style-type: none"> <li>Consider serotonin antagonists (ie, dolasetron, granisetron, ondansetron, palonosetron, tropisetron), short-term corticosteroids (ie, dexamethasone, prednisone), or other antiemetics. See <a href="#">NCCN Guidelines for Antiemesis</a>.</li> </ul>
<b>Histamine-2 receptor blockers<sup>7</sup>:</b> • famotidine • ranitidine • cimetidine	<ul style="list-style-type: none"> <li>Delirium</li> <li>Cognitive impairment</li> <li>Can worsen dementia</li> </ul>	<ul style="list-style-type: none"> <li>Avoid in patients at risk for delirium.</li> </ul>	<ul style="list-style-type: none"> <li>Proton pump inhibitors (eg, omeprazole, esomeprazole, pantoprazole, lansoprazole)</li> <li>An alternative to H2 blockers may be antacids such as calcium carbonate, in addition to proton pump inhibitors, if hypercalcemia of malignancy is not a concern.</li> </ul>

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Note: All recommendations are category 2A unless otherwise indicated.

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## Older Adult Oncology

### MEDICATIONS COMMONLY USED FOR SUPPORTIVE CARE THAT ARE OF CONCERN IN OLDER PATIENTS

Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
<b>Selective serotonin reuptake inhibitor (SSRI) antidepressants<sup>4,5,7,8,10</sup>:</b> • fluoxetine • paroxetine • sertraline • fluvoxamine • citalopram • escitalopram	<ul style="list-style-type: none"> <li>Can induce ataxia, impair psychomotor function</li> <li>Increases risk for syncope</li> <li>Increases risk for falls</li> <li>Exacerbates hyponatremia, particularly in older adults by syndrome of inappropriate antidiuretic hormone secretion (SIADH)</li> <li>Increases risk for GI bleeding, particularly when using with nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, or anticoagulation</li> <li>Can increase QT interval</li> </ul>	<ul style="list-style-type: none"> <li>Consider side-effect profile and drug interactions prior to the selection of antidepressants.</li> <li>Review the need for continued treatment for depression at least 6 months after remission of the episode, based on number of prior episodes, residual symptoms, current medical problems, and psychosocial difficulties.</li> <li>Consider stopping by gradually reducing the dose over a 4-week period in patients who no longer need antidepressants.</li> <li>Avoid in patients with falls, unless alternatives are not available.</li> <li>Avoid in patients with SIADH.</li> <li>Avoid paroxetine (and possibly fluoxetine) in patients taking tamoxifen.</li> <li>Consider baseline electrocardiogram (ECG) before initiation of therapy.</li> </ul>	<ul style="list-style-type: none"> <li>For patients with falls, consider SNRIs (eg, venlafaxine, desvenlafaxine, duloxetine) or bupropion.</li> <li>Consider the use of a gastroprotective medication (proton pump inhibitors such as omeprazole, esomeprazole, or misoprostol) if SSRIs must be combined with NSAIDs, aspirin, or antiplatelet agents.</li> <li>For patients taking warfarin, heparin, or anticoagulants, consider mirtazapine.</li> <li>Consider complementary or alternative therapy (eg, CBT).</li> </ul>

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Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
<b>Antipsychotics<sup>4,5,7,8,11-14:</sup></b> • chlorpromazine • fluphenazine • haloperidol • loxapine • molindone • perphenazine • pimozide • promazine • thioridazine • thiothixene • trifluoperazine • triflupromazine • aripiprazole • asenapine • clozapine • iloperidone • lurasidone • olanzapine • paliperidone • quetiapine • risperidone • ziprasidone	<ul style="list-style-type: none"> <li>Some agents have anti-anticholinergic effects (especially chlorpromazine, clozapine, loxapine, olanzapine, thioridazine, and trifluoperazine)</li> <li>Increased risk of cerebrovascular accident (CVA)</li> <li>Increased risk of mortality in patients with dementia</li> <li>Hyperglycemia</li> <li>Increased risk of falls and fractures, especially in patients at risk</li> <li>Concern for QT prolongation, especially in combination with serotonin antagonists, antidepressants, and in patients with underlying cardiac diseases</li> </ul>	<ul style="list-style-type: none"> <li>In the presence of psychosis and danger to self/others, use low-dose non-anticholinergic agent for the shortest duration possible.</li> <li>May be appropriate for short-duration treatment of refractory chemotherapy-induced nausea and vomiting.</li> <li>May be appropriate for short-term management of delirium or for patients with severe agitation, which will result in interruption of essential medical therapies or poses a danger for self-injury; or for those with distressing psychotic symptoms (eg, hallucinations, delusions).</li> <li>With concern for QT prolongation, start at the lowest dose with slow uptitration. Consider baseline ECG before initiation of therapy.</li> </ul>	<ul style="list-style-type: none"> <li>For delirium, short-term use (no more than 5 days) of one of the following at low dose:           <ul style="list-style-type: none"> <li>Haloperidol<sup>a</sup> (0.25–1 mg PO up to every 8 hours)</li> <li>Olanzapine<sup>a</sup> (2.5–5 mg PO daily)</li> <li>Risperidone<sup>a</sup> (0.25–0.5 mg PO daily)</li> <li>For patients with parkinsonism, quetiapine<sup>a</sup> (12.5–25 PO daily or every 12 hours)</li> </ul> </li> <li>If using an antipsychotic, attempt to reduce, taper, or stop other antipsychotics and/or drugs acting on the CNS that can worsen the risk of falls or cognitive decline.</li> <li>For nausea, consider other antiemetics (serotonin antagonists such as ondansetron, dexamethasone, or aprepitant) if risk outweighs the benefit of using an antipsychotic.</li> <li>Monitor for extrapyramidal symptoms; tools such as the Abnormal Involuntary Movement Scale are useful.</li> <li>See <a href="#">NCCN Guidelines for Antiemesis</a></li> </ul>

[Continued](#)[References](#)<sup>a</sup> Unlabeled use.

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**MEDICATIONS COMMONLY USED FOR SUPPORTIVE CARE THAT ARE OF CONCERN IN OLDER PATIENTS**

Consider initiating all medications at the lowest possible dose and increase dose gradually (as tolerated).

Therapeutic Class/ Medication(s)	Negative Effects/ Condition the Drug May Adversely Affect	Recommendation	Alternative(s)
<b>Antiepileptic drugs (AEDs)<sup>15</sup>:</b> • phenobarbital • primidone • phenytoin • carbamazepine	<ul style="list-style-type: none"> <li>Induce multiple cytochrome P450 enzymes, resulting in clinically significant drug interactions</li> <li>Falls</li> </ul>	<ul style="list-style-type: none"> <li>Avoid for newly diagnosed epilepsy in persons aged ≥60 years not currently on antiepileptic therapy, unless at least two other AEDs have been unsuccessful in stopping seizures or have intolerable adverse effects.</li> <li>Carefully check drug interactions when using these agents.</li> </ul>	<ul style="list-style-type: none"> <li>Examples of multiple AEDs that do not induce cytochrome P450 enzymes: lamotrigine, levetiracetam, tiagabine, and topiramate.</li> </ul>
<b>Opioids<sup>16-19</sup></b> • morphine • codeine • tramadol • hydrocodone • oxycodone • hydromorphone • fentanyl • methadone • buprenorphine	<ul style="list-style-type: none"> <li>Sedation</li> <li>Impaired balance and falls</li> <li>Nausea/vomiting</li> <li>Constipation</li> <li>Respiratory depression, especially in patients with sleep apnea</li> <li>Urinary retention</li> <li>Dependence</li> <li>Long-term use is associated with bone loss</li> <li>Confusion</li> <li>Delirium</li> </ul>	<ul style="list-style-type: none"> <li>Start low and escalate slowly, use longer intervals.</li> <li>Start with short-acting agents.</li> <li>Make sure patients are on a bowel regimen to avoid severe constipation.</li> <li>Caution when prescribing with underlying dementia.</li> <li>Half-life may be longer in older adults who have renal or hepatic dysfunction.</li> <li>Buprenorphine is the preferred agent in older adults requiring long-acting opioids.</li> </ul>	<ul style="list-style-type: none"> <li>Consider using nonopioids if possible; NSAIDs, acetaminophen</li> <li>Consider radiation or nerve block in localized pain</li> <li>For neuropathic pain, consider non-opioids</li> <li>See <a href="#">NCCN Guidelines for Adult Cancer Pain</a></li> </ul>

**References**

Note: All recommendations are category 2A unless otherwise indicated.



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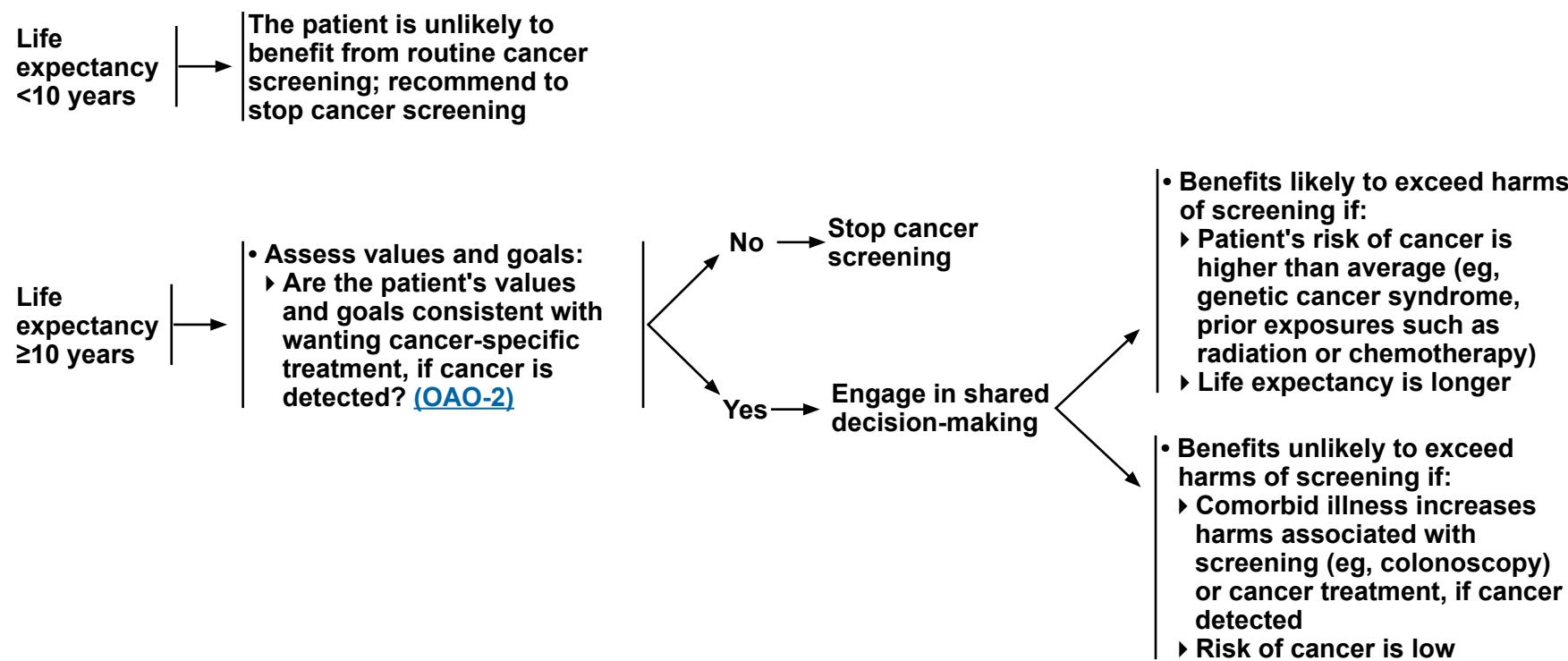
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- <sup>18</sup> Vadivelu N, Hines RL. Management of chronic pain in the elderly: focus on transdermal buprenorphine. Clin Interv Aging 2008;3:421-430.
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## APPROACH TO CANCER SCREENING FOR OLDER ADULT CANCER SURVIVORS

Note: “Cancer screening” refers to screening for new primary cancers different than the cancer survivor’s prior cancer(s). There is evidence to support routine screening for the following cancers (although evidence in older individuals is limited): breast, colorectal, and lung cancer. There is limited or no evidence to support screening for cervical cancer or prostate cancer in older adults. For specific cancer screening recommendations, including NCCN recommendations regarding the early detection of prostate cancer, please refer to the respective [NCCN Guidelines for Detection, Prevention, and Risk Reduction](#).

### Is the cancer survivor a candidate for routine cancer screening considering overall life expectancy?<sup>a</sup>



<sup>a</sup> Refer to life table and eprognosis ([OAO-A](#)). See [NCCN Guidelines for Survivorship](#) for the definition of survivorship and standards for survivorship care.

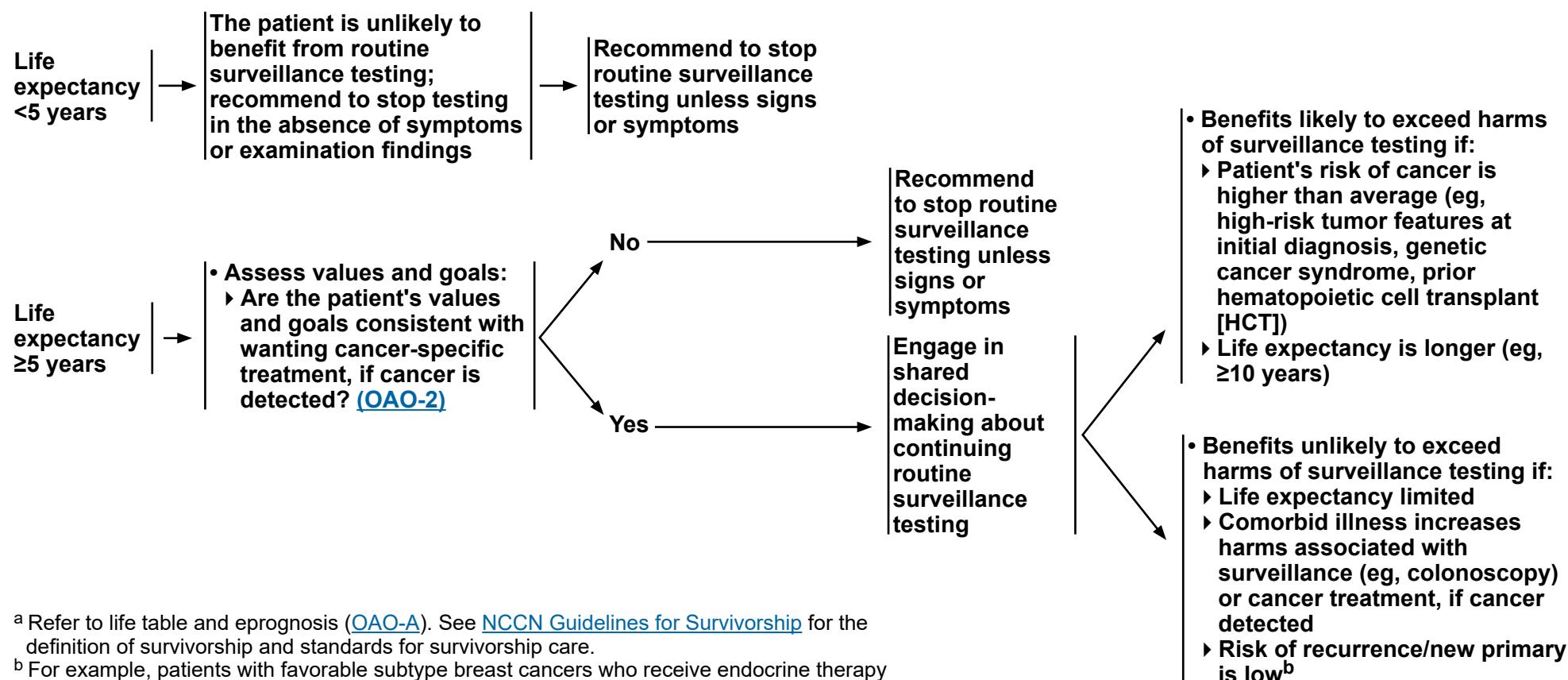
**Note:** All recommendations are category 2A unless otherwise indicated.



## APPROACH TO SURVEILLANCE TESTING FOR OLDER ADULT CANCER SURVIVORS WITH NO EVIDENCE OF DISEASE

“Surveillance testing” refers to routine assessment (in the absence of symptoms or examination findings) for recurrence or new primary cancers of the same type as the cancer survivor’s prior cancer(s) beyond routine history and physical examination.  
(Note that patients with symptoms or signs suspicious for cancer on history or physical examination should undergo diagnostic evaluation.)

**Is the cancer survivor a candidate for routine surveillance testing considering overall life expectancy?<sup>a</sup>**



<sup>a</sup> Refer to life table and eprognosis ([OAO-A](#)). See [NCCN Guidelines for Survivorship](#) for the definition of survivorship and standards for survivorship care.

<sup>b</sup> For example, patients with favorable subtype breast cancers who receive endocrine therapy have a lower risk of recurrence/new primaries than similarly aged patients with no history of breast cancer (Freedman RA, et al. JAMA Oncol 2021;7:609-615).

Note: All recommendations are category 2A unless otherwise indicated.



## CONSIDERATIONS FOR CAREGIVERS OF OLDER ADULTS WITH CANCER

### **Role of Caregivers in Oncology for Older Adults**

- Caregivers often provide essential support in daily living, medical care, and social needs, including practical assistance (eg, transportation, meal preparation), physical care (eg, bathing, toileting), medical care (eg, medication management, wound care), social care (eg, companionship), and financial management.
- Caregivers serve as advocates by helping patients navigate medical decisions and helping to coordinate their care with clinicians and insurers.

### **Assessing the Needs and Burden of Caregivers for Older Adults**

- Caregivers can experience a substantial emotional toll, as well as physical and psychological stress. Capacity for caregiving and threshold for feeling overwhelmed varies between individuals.
- Caregivers' physical and mental well-being should be periodically assessed by exploring their confidence in providing care and their need for additional resources or support.
- Caregivers may not openly express their struggles, so questions like, "How are you managing your responsibilities?" or "Do you need help but are reluctant to ask?" can initiate meaningful dialogue.
- Cancer care teams should evaluate caregivers' willingness and ability to assume care responsibilities, and should reassess these responsibilities regularly as patient needs evolve (eg, post-hospital discharge, disease progression).
  - ▶ Validated caregiver burden assessment tools: (eg, [Zarit Burden Interview](#), [Caregiver Strain Index](#)).

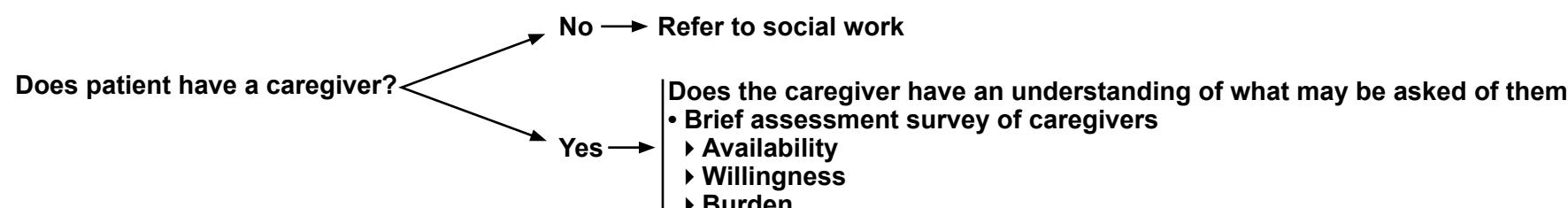
### **Strategies for Caregivers Support**

- **Education and Training:** Provide tailored education on cancer management, and expectations of caregivers when treatment planning.
- **Involving Caregivers in Treatment Decisions:** Consider the patient's and caregiver's ability to manage care at home. Include caregivers in advance care planning discussions so that the care plan aligns with the patient's and family's wishes.
- **Access to Community and Professional Support:** Encourage caregivers to seek support through volunteer or paid services, caregiver support groups, and licensed social workers. Consider non-medical home care services (eg, housekeeping, meal preparation, transportation) and medical services (eg, home health care). Spiritual care through chaplaincy services may also be appropriate for some families.
  - ▶ Direct to resources for caregiver support: [Family Caregiver Alliance's toolkit](#).
- **Telehealth and Resource Utilization:** Telehealth services and mail-order pharmacies can reduce travel burden and associated costs.
- **Addressing Caregiver Burnout:** Periodically assess for signs of caregiver burnout and offer respite care services or alternative care arrangements when necessary.
- **Supporting Caregivers:** Caregivers may neglect their own well-being and should be reminded to attend to their own health.

Note: All recommendations are category 2A unless otherwise indicated.



### APPROACH TO ASSESSING CAREGIVER STATUS



Domain	Assessment Tools/Description	Additional Assessments/Potential Interventions
Caregiver Assessment	<ul style="list-style-type: none"> <li>Evaluate caregiver stress and burden           <ul style="list-style-type: none"> <li><a href="#">Zarit Burden Interview</a></li> <li><a href="#">Caregiver Reaction Scale</a></li> <li><a href="#">Caregiver Self-Assessment Questionnaire</a></li> </ul> </li> <li>Evaluate caregiver coping           <ul style="list-style-type: none"> <li><a href="#">Revised Scale for Caregiving Self-Efficacy</a></li> <li><a href="#">Perceived Support Scale</a></li> <li><a href="#">Cultural Justification for Caregiving Scale</a></li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Consider referrals to social work for:           <ul style="list-style-type: none"> <li>Therapeutic counseling</li> <li>Respite care resources</li> <li>Financial burden</li> <li>Resources for support services</li> <li>Caregivers of patients with cognitive impairment</li> <li>Bereavement care</li> </ul> </li> <li>Helpful resources:           <ul style="list-style-type: none"> <li><a href="https://www.caregiving.org/resources">https://www.caregiving.org/resources</a></li> <li>Cancer support community helpline: 1.888.793.9355 or to chat live at <a href="http://www.cancersupportcommunity.org">www.cancersupportcommunity.org</a></li> </ul> </li> <li>Clinicians can support caregivers by using guided, open-ended questions that focus on how the caregiver is handling the situation. This can help us connect them to the appropriate resources to help alleviate caregiver burden.</li> </ul>

Note: All recommendations are category 2A unless otherwise indicated.



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### CONSIDERATIONS FOR CAREGIVERS OF OLDER ADULTS WITH CANCER

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Note: All recommendations are category 2A unless otherwise indicated.

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### ABBREVIATIONS

aCGA	Abbreviated Comprehensive Geriatric Assessment	G-8	Geriatric 8	OARS	Older Americans Resources and Services
ADL	activities of daily living	GA	geriatric assessment	OT	occupational therapy
AED	antiepileptic drug	GEMS	Geriatrics Evaluation & Management Tools	PT	physical therapy
AGS	American Geriatrics Society	GI	gastrointestinal	QOL	quality of life
BMD	bone mineral density	GSV	Geriatric Surgery Verification	SABR	stereotactic ablative radiotherapy
BMI	body mass index	HCT-CI	Hematopoietic Cell Transplantation-Specific Comorbidity Index	SAOP	Senior Adult Oncology Program
BOMC	Blessed Orientation Memory Concentration Test	IADL	instrumental activities of daily living	SIADH	syndrome of inappropriate antidiuretic hormone secretion
CAR	chimeric antigen receptor	IGRT	image-guided radiation therapy	SLUMS	Saint Louis University Mental Status Exam
CARG	Cancer and Aging Research Group	IMRT	intensity-modulated radiation therapy	SNRI	serotonin-norepinephrine reuptake inhibitor
CARG-BC	Cancer and Aging Research Group-Breast Cancer	irAE	immune-related adverse event	SPPB	Short Physical Performance Battery
CBT	cognitive behavioral therapy	LVEF	left ventricular ejection fraction	SRH	Self-Rated Health
CCI	Charlson Comorbidity Index	MAI	Medication Appropriateness Index	SSRI	selective serotonin reuptake inhibitor
CHF	congestive heart failure	MMSE	Mini-Mental State Examination	START	Screening Tool to Alert to Right Treatment
CIRS-G	Cumulative Illness Rating Scale-Geriatric	MNA	Mini-Nutritional Assessment	STOPP	The Screening Tool of Older Persons' Prescriptions
CNS	central nervous system	MoCA	Montreal Cognitive Assessment	TRST	Triage Risk Screening Tool
CRASH	Chemotherapy Risk Assessment Scale for High-Age Patients	MOS	Medical Outcomes Study	TSH	thyroid-stimulating hormone
CVA	cerebrovascular accident	NSAID	nonsteroidal anti-inflammatory drug	TUG	Timed Up and Go
ECG	electrocardiogram	NSQIP	National Surgical Quality Improvement Program	VES-13	Vulnerable Elders Survey
ECOG	Eastern Cooperative Oncology Group				



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### NCCN Categories of Evidence and Consensus

<b>Category 1</b>	Based upon high-level evidence ( $\geq 1$ randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus ( $\geq 85\%$ support of the Panel) that the intervention is appropriate.
<b>Category 2A</b>	Based upon lower-level evidence, there is uniform NCCN consensus ( $\geq 85\%$ support of the Panel) that the intervention is appropriate.
<b>Category 2B</b>	Based upon lower-level evidence, there is NCCN consensus ( $\geq 50\%$ , but $< 85\%$ support of the Panel) that the intervention is appropriate.
<b>Category 3</b>	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise indicated.



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### Discussion

This discussion corresponds to the NCCN Guidelines for Older Adult Oncology.  
Last updated on July 12<sup>th</sup>, 2022.

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### Overview

Cancer is the leading cause of death in patients aged 60 to 79 years.<sup>1</sup> More than 50% of all cancers and more than 70% of cancer-related deaths in the United States occur in patients who are 65 years and older.<sup>2</sup> It is estimated that by 2030 approximately 70% of all cancers will be diagnosed in adults aged 65 years and older.<sup>3</sup> Aging in the U.S. population and greater life expectancy mean that cancer in older adults is becoming an increasingly common problem. Furthermore, older patients with cancer are under-represented in clinical trials for new cancer therapies.<sup>4</sup> Therefore, less evidence-based information exists to guide the treatment of these patients.

The challenge of managing older patients with cancer is to assess whether the expected benefits of treatment are superior to the risks in a population with decreased life expectancy and decreased tolerance to stress. There are unique issues to consider when caring for an older adult with cancer. The biological characteristics of certain cancers and their responsiveness to therapy are different in older patients compared to their younger counterparts.<sup>5</sup> In addition, older patients have decreased tolerance to anticancer therapy. Nevertheless, advanced age alone should not be the only criterion to preclude effective treatment that could improve quality of life (QOL) or lead to a survival benefit in older patients.<sup>6,7</sup> The available data suggest that older patients with good performance status can tolerate commonly used chemotherapy regimens as well as younger patients, particularly when adequate supportive care is provided.<sup>8-10</sup> However, there have been few studies that have addressed patients at the extremes of age or those with poor performance status. Multidisciplinary team management, a patient-specific treatment approach with shared decision-making, and palliative/supportive care for symptom management should be an integral part of cancer care in older adults.

Together, these age-related issues form the basis for the development of Guidelines that address special considerations in older adults with cancer. Proper selection of patients is the key to administering effective and safe cancer treatment. Treatment that diminishes QOL with no significant survival benefit should be avoided. The physiologic changes associated with aging may impact an older adult's ability to tolerate cancer therapy and should be considered in the treatment decision-making process. The NCCN Guidelines® for Older Adult Oncology address specific issues related to the management of cancer in older adults, including screening and comprehensive geriatric assessment (CGA), assessing the risks and benefits of treatment, preventing or decreasing complications from therapy, and managing patients deemed to be at high risk for toxicity from standard treatment.

### Literature Search Criteria and Guidelines Update Methodology

Prior to the update of this version of the NCCN Guidelines for Older Adult Oncology, a literature search was performed to obtain key literature in Older Adult Oncology using the following search terms: older patients and cancer, treatment, allogeneic stem cell transplantation, adherence, comprehensive geriatric assessment, toxicity and chemotherapy, polypharmacy, comorbidities, functional status, cognitive status, nutritional status, falls, frailty, geriatric syndromes, delirium, dementia, depression, and distress.

The search results were narrowed by selecting studies in humans published in English. Results were confined to the following article types: Clinical Trial, Phase II; Clinical Trial, Phase III; Clinical Trial, Phase IV; Guideline; Randomized Controlled Trial; Meta-Analysis; Systematic Reviews; and Validation Studies.



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The data from key PubMed articles selected by the panel for review during the Guidelines update meeting as well as articles from additional sources deemed as relevant to these Guidelines and discussed by the panel have been included in this version of the Discussion section. Recommendations for which high-level evidence is lacking are based on the panel's review of lower-level evidence and expert opinion.

NCCN recommendations have been developed to be inclusive of individuals of all sexual and gender identities to the greatest extent possible. When citing data and recommendations from other organizations, the terms men, male, women, and female will be used to be consistent with the cited sources.

The complete details of the Development and Update of the NCCN Guidelines are available at [www.NCCN.org](http://www.NCCN.org).

### Approach to Shared Decision-Making in Older Patients Prior to Cancer-Specific Treatment

Older patients can be classified into three categories: 1) young old patients are 65 to 75 years of age; 2) old patients are 76 to 85 years of age, and 3) oldest old patients are older than 85 years of age.<sup>5</sup> Chronologic age by itself is not reliable in estimating life expectancy, functional reserve, or the risk of treatment complications.<sup>11</sup> While it is not possible for a physician to predict the exact life expectancy of an individual patient, it is possible to provide an estimate of whether a patient is likely to live longer or shorter than an average person of similar age.<sup>12-18</sup>

Life expectancy at a given age can be estimated using life table data as suggested by Walter and Schonberg.<sup>19</sup> For example, about 25% of the healthiest 75-year-old patient will live more than 22 years, 50% will live at least 17 years, and 25% will live less than 10 years. Lee and colleagues developed and validated a potentially useful tool for clinicians to estimate

the 4-year mortality risk.<sup>14</sup> Patients can be stratified into three groups of varying risk of mortality (high, intermediate, or low) based on the prognostic index, which incorporates demographic variables (age and sex), self-reported comorbid conditions and functional measures.<sup>14</sup> Carey and colleagues also developed a similar functional morbidity index based on self-reported functional status, age, and gender to stratify elders into varying risk groups for 2-year mortality.<sup>13</sup>

The risk of morbidity from cancer is generally established by the stage at diagnosis, the aggressiveness of the tumor, and the risk of recurrence and progression. More generally, a useful collection of tools to estimate the general mortality risk in older adult can be found online at <https://eprognosis.ucsf.edu>. Life expectancy calculators available on this website can be utilized to determine anticipated life expectancy (independent of cancer) and in clinical decision-making to assess whether 1) the cancer is likely to shorten the patient's life expectancy; or 2) whether the patient is likely to become symptomatic from cancer during the anticipated life expectancy. These calculators should be used in conjunction with clinical judgment.

Patients with a low risk of dying or suffering from their cancer and who have other competing causes of mortality can receive symptom management and supportive care as detailed in the appropriate NCCN Guidelines for Supportive Care. Patients who are at moderate or high risk of suffering from their cancer can be further evaluated to assess their functional dependency, decision-making capacity, overall goals, and desire for the proposed treatment.<sup>20,21</sup>

A patient's decision-making capacity is generally evaluated based on the patient's ability to understand the relevant information about the diagnosis and proposed cancer-specific diagnostic tests or treatment options; appreciate their underlying values and current medical situation; use



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reason to make decisions; and communicate a consistent choice. It is essential that key concepts and information regarding the diagnosis of cancer and cancer-specific treatment be communicated to older patients in a way that they can understand. See *Optimizing Communication with Older Adults* in the algorithm. Sessums et al evaluated a variety of instruments used to assess medical decision-making capacity in adult patients without mental illness and concluded that Aid to Capacity Evaluation (ACE) is the best available instrument to assist physicians in making assessments about a patient's medical decision-making capacity.<sup>21</sup>

Irrespective of age, a person who is functionally independent without serious comorbidities and has good decision-making capacity should be a candidate for most forms of cancer-specific treatment. Patient's goals and objectives should be assessed in context of life expectancy; comorbidities; cognitive, functional, psychological/psychosocial, and nutritional status; aggressiveness of the disease; and treatment approach. There are data to suggest a correlation between low social support and a higher risk for mortality. In patients with low levels of social support, referral to social work should be considered and/or case management to explore home supports and community resources. Multidisciplinary team management, patient-specific treatment approach with shared decision-making, and palliative/supportive care for symptom management should be an integral part of cancer care in older adults. In patients without decision-making capacity, the Guidelines recommend considering consultation with a social worker, psychologist, palliative care specialist, or an ethics committee. Additional information can be obtained from the patient's proxy, advance directive/advance care planning document, health care power of attorney, living will, or clinician's documentation.

Functionally independent patients with contraindications to treatment and patients with major functional impairment with or without complex comorbidity should be managed according to the appropriate NCCN Guidelines for Supportive Care. Patients who are dependent in some instrumental activities of daily living (IADLs), with or without severe comorbidities, are at increased risk of cancer-specific treatment complications. For these patients with intermediate functional impairment who have milder problems (such as dependence in one or more IADLs, milder comorbidity, depression, minor memory disorder, mild dementia, and inadequate caregiver), treatment may still be administered with special individualized precautions.<sup>5</sup>

The potential benefits of cancer-specific treatments include prolonged survival, and improvement of QOL and function, as well as palliation of symptoms. For patients who are able to tolerate treatment, options include surgery, radiation therapy (RT), chemotherapy, targeted therapies, and immunotherapy.

### Pre-Treatment Evaluation

The NCCN Older Adult Oncology Panel recommends pre-treatment evaluation using a CGA for all older adults with cancer, especially if there are apprehensions regarding the patient's ability to tolerate treatment. The CGA is a multidisciplinary, in-depth evaluation that assesses the objective health of the older adult through evaluation of multiple domains, which predict overall prognosis as well as fitness and ability to tolerate cancer therapy. The feasibility of conducting a CGA in oncology practice has been demonstrated among older patients with cancer in clinical practice and research settings.<sup>22-24</sup> The components of CGA, including comorbid conditions, functional status, cognitive function, geriatric syndromes, polypharmacy, and nutritional status, have been associated with survival and chemotherapy tolerance.<sup>25-34</sup>



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For example, in patients 65 years or older diagnosed with stage I–III primary breast cancer, the all-cause and breast-cancer-specific death rates at 5 and 10 years were consistently approximately two times higher in patients with three or more cancer-specific CGA deficits, regardless of age and stage of disease.<sup>28</sup> In another prospective study of 375 consecutive older patients with cancer (ELCAPA study), in a multivariate analysis, a lower activities of daily living (ADLs) score and malnutrition were independently associated with changes in the cancer treatment intensity.<sup>29</sup> In a prospective multicenter study of 348 previously untreated cancer patients older than 70 years, poor nutritional status, impaired mobility, and advanced tumors were identified as risk factors predictive of early death (<6 months) after initiation of chemotherapy.<sup>30</sup> In a phase III study (FFCD 2001-02), impairment in functional status and cognitive function (as assessed by IADLs and Mini-Mental State Exam [MMSE], respectively) were predictive of severe chemotherapy-related toxicity and hospitalization in older patients with metastatic colorectal cancer (CRC).<sup>31</sup> Similarly, among older patients receiving induction chemotherapy for acute myeloid leukemia (AML), overall survival (OS) was significantly shorter for patients with impaired cognitive and physical function.<sup>32</sup> CGA has also been reported to be an efficient method to identify older patients with diffuse large B-cell lymphoma (DLBCL) who can benefit from anthracycline-based chemoimmunotherapy.<sup>27,35</sup>

Although CGA is helpful for physicians to develop a coordinated plan for cancer treatment as well as to guide appropriate interventions to address problems that were identified during assessment, it can be time-consuming and may not be practical for all patients. Geriatric screening assessment tools can be used to identify older adults with cancer who would benefit from a full CGA. At a minimum, assessment using a geriatric screening tool is recommended for older adults with cancer prior to treatment initiation.

### Geriatric Screening Tools

Multiple geriatric screening tools have been tested and validated to identify patients at risk who would benefit from a CGA. The Geriatric 8 (G8),<sup>36,37</sup> modified G8,<sup>38</sup> and Vulnerable Elders Survey (VES-13)<sup>39-42</sup> are the most commonly used screening tools to identify older adults with cancer who would benefit from a CGA.<sup>43,44</sup>

The abbreviated CGA (aCGA),<sup>45,46</sup> Barber questionnaire,<sup>47</sup> Fried Frailty Criteria,<sup>48,49</sup> Groningen Frailty Index,<sup>46</sup> Triage Risk Screening Tool (TRST),<sup>37</sup> Lachs' screening test,<sup>50</sup> and Senior Adult Oncology Program 2 (SAOP2)<sup>51,52</sup> have also been used to identify patients who would benefit from a CGA.

The SAOP2 screening tool developed by Extermann and colleagues is aimed at identifying older patients who would benefit from a multidisciplinary evaluation by a geriatric oncology team. The SAOP2 screening tool includes the assessment of older cancer patients across the following domains using validated measures: self-rated health, cognitive function, nutritional status, comorbidity, ECOG performance status, and functional status.

G8 and aCGA were developed specifically for older patients with cancer. In a systematic review, Hamaker et al assessed the sensitivity and specificity of frailty screening methods that could potentially be useful in the selection of patients for CGA.<sup>53</sup> G8 and TRST had the highest sensitivity (87% and 92%, respectively) and aCGA had the highest specificity (97%) for predicting frailty on CGA. A modified six-item version of the G8 screening tool, which was evaluated in a prospective cohort of older patients with cancer from the ELCAPA study, exhibited better diagnostic performance with 89% sensitivity and 79% specificity.<sup>38</sup> In the ONCODAGE prospective multicenter cohort study, which evaluated the diagnostic accuracy of G8 and VES-13 as predictive screening tools to identify older patients who would require CGA, G8 was more sensitive and VES-13 was more specific. Abnormal G8 score, advanced stage,



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male sex, and poor performance status were independent prognostic factors of 1-year survival.<sup>44</sup>

While all of the screening tools included the assessment of functional status, the assessment of other domains such as psychosocial status, nutritional status, comorbidities, and polypharmacy varied widely. For example, aCGA, Fried Frailty Criteria, and VES-13 had a stronger predictive value for impairment of functional status (ADLs and IADLs) and G8 had a strong predictive value for nutritional status, but not for other geriatric conditions. As a result, none of the screening tools was successful in identifying impairments across all of the domains included in CGA. Given the lack of data supporting the use of any one screening tool for predicting outcome of a CGA, screening tools should not replace CGA in the management of older patients with cancer. However, screening tools could be used to identify those patients who would benefit from a CGA prior to initiation of therapy.<sup>43,54</sup> In a systematic review of skin cancer patients screened using different frailty screening tools, G8 appeared to be the best tool for assessing frailty although more data are needed to assess its feasibility in the clinic for this patient population.<sup>55</sup> The appropriate use of geriatric screening tools and/or CGA (as described below) enables physicians to develop a coordinated plan for cancer treatment and to guide interventions tailored to the individual patient.

### Comprehensive Geriatric Assessment

The CGA is a multidisciplinary, in-depth evaluation that assesses the objective health of the older adult while evaluating multiple domains, which informs cancer prognosis and predicts treatment tolerance. The appropriate use of geriatric screening tools and/or CGA enables physicians to develop a coordinated plan for cancer treatment and to guide interventions tailored to the individual patient. The CGA includes assessment tools that evaluate the functional age of older patients with cancer based on function and mobility, comorbidities that may interfere

with cancer treatment, polypharmacy, nutritional status, cognitive function, psychological status, socioeconomic issues, and various geriatric syndromes.

CGA can reveal reversible geriatric problems that are not detected by routine oncology care and predict toxicity from cancer treatment. Identifying these issues can enable targeted use of supportive care measures to improve QOL and ensure compliance with adherence to therapy.<sup>56-58</sup> Some components of CGA have also been incorporated in tools that have been developed to predict the risk of severe toxicity from chemotherapy in older patients with cancer (eg, Cancer and Aging Research Group [CARG] Chemo Toxicity Calculator and Chemotherapy Risk Assessment Scale for High-Age Patients [CRASH] score; See *Considerations for Older Adults Undergoing Cancer-Specific Treatment - Systemic Therapy* in the algorithm).<sup>59-61</sup> The CGA may also be useful in estimating life expectancy, which is of paramount importance when making treatment decisions, and allowing for shared decision-making with the patient and/or the caregiver. Furthermore, CGA can also promote improved communication with patients and caregivers.<sup>62</sup>

Older adults may benefit from a referral to a geriatric-trained clinician for risk stratification prior to cancer treatment, to develop a coordinated plan of care with the oncologist and/or to manage geriatric syndromes that could jeopardize outcomes of cancer treatment. The geriatric-trained clinician thus may be able to assist the oncologist in optimizing the management of non-cancer aspects of the patient's care, which in turn may enable more effective delivery of direct cancer care. Consultation with a geriatric-trained clinician should be considered for the following: cognitive impairment (dementia/delirium, decision-making capacity evaluation, life expectancy, advance directive/advance care planning, and guardianship), functional/physical impairment, vision/hearing impairments, polypharmacy, when considering high-risk procedures, geriatric



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syndromes (ie, repeated falls, incontinence), weight loss, and social and caregiver support.

Although typically a thorough CGA is performed by a geriatric-trained clinician, many of the tools can be incorporated into routine practice and administered by providers without any advanced training in this area. The various domains of CGA and the recommended tools for their assessment are discussed below.

### Function Status and Mobility

Functional status and mobility in older adults with cancer may be evaluated using either self-reported assessments tools or objective measures. Self-reported assessment tools include ADLs, IADLs, and the number of falls within the past 6 months.<sup>63,64</sup> ADLs encompass basic self-care skills required to maintain independence at home (eg, bathing, using the bathroom) and IADLs encompass complex skills that are necessary for maintaining independence in the community (eg, shopping). The need for assistance with IADLs has been associated with decreased treatment tolerance and poorer survival in older patients with cancer.<sup>25-27,65</sup> Objective measures such as the Timed Up and Go (TUG) test, the Timed 10-Meter Walk Test (or gait speed), and the Short Physical Performance Battery (SPPB) test can also be used to assess function and mobility in older patients.

The TUG test is a quick screening test to assess mobility and overall motor function in older adults.<sup>66,67</sup> The TUG test score is calculated as the time in seconds it takes for a patient to stand up from an armchair without using his or their arms, walk 10 feet forward at his or her usual pace, turn around, walk back to the chair, and then sit down again. The patient may use an assistive device, such as a cane or walker, but may not have assistance from another person. The TUG test score has been shown to predict the risk of falls in older adults.<sup>68,69</sup> In a preliminary prospective

study, the TUG test was also associated with good sensitivity and specificity in the assessment of falls in older patients with cancer.<sup>70</sup> A TUG test score of 13 seconds or greater is associated with an increased risk of falls. For these patients, a comprehensive evaluation should be considered. The NCCN Older Adult Oncology Panel recommends including evaluation of ADLs, IADLs, and at least one other objective measure of function and mobility when assessing an older adult with cancer before treatment. See *Falls Assessment and Interventions* in the algorithm. Gait speed has also been used to assess functional status and health outcomes in older adults.<sup>17,71</sup> It has been reported that decline in gait speed (slow, moderate, and fast) could predict mortality in well-functioning older adults.<sup>16</sup> In a pooled analysis of individual data from 9 large cohort studies that included more than 30,000 participants ( $\geq 65$  years) living in the community, Studenski and colleagues reported that gait speed was associated with survival in older adults.<sup>15</sup> In this analysis, with 0.8 meter/second as the cutoff, gait speed faster than 1.0 meter/second suggested a better-than-average life expectancy and gait speed faster than 1.2 meters/second suggested exceptional life expectancy. White and colleagues reported that decline in gait speed (slow, moderate, and fast) could predict mortality in well-functioning older adults. A fast decline in gait speed was associated with a 90% greater risk of mortality than a slow decline.<sup>16</sup> The predictive value of gait speed has also been evaluated in older patients with cancer.<sup>72,73</sup> In the Health, Ageing and Body Composition study that included 429 older patients with cancer, faster gait speed (time taken to cover a 20-meter course) was associated with lower risk of death (hazard ratio [HR] = .89) in patients with metastatic cancer and lower 2-year progression to death or disability in patients with non-metastatic cancer.<sup>72</sup> In the Physical Frailty in Elder Cancer patients study that included 190 patients (mean age, 80.6 years) with cancer during the first 6 months following a CGA, a gait speed slower than 0.8 meter/second (HR, 5.6; 95% CI, 1.6–19.7;  $P = .007$ ) was significantly associated with early death.<sup>73</sup> Gait speed may be helpful in identifying



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older patients with a longer life expectancy and who may be candidates for preventive interventions that are associated with long-term benefit.

The SPPB is a tool used to assess lower extremity function and mobility in older adults by measuring gait speed, balance, and strength.<sup>74</sup> Several studies have validated its ability to predict mobility disability, frailty, ADL disability, nursing home admission, hospitalization, and mortality.<sup>75-78</sup> In a prospective cohort study, 1122 individuals aged 71 years or older (with no ADL limitations, the ability to walk one-half mile, and the ability to climb stairs without assistance) were instructed to perform tasks relating to the SPPB and follow-up after a period of 4 years. It was found that lower scores on the SPPB were associated with statistically significant disabilities at follow-up. In fact, those with lower scores at onset were 4.2 to 4.9 times more likely to have a disability at follow-up.<sup>75</sup> In another study, the association between the SPPB and the loss of the ability to walk 400 meters was evaluated. A total of 542 individuals aged 65 years and older completed the SPPB and 400-meter walk at baseline and following a period of 3 years. It was found that a lower SPPB score ( $\leq 10$  at baseline) was strongly predictive of mobility disability at follow-up (OR, 3.38, 95% CI, 1.32–8.65).<sup>76</sup>

Interventions in the case of limitations in function and mobility are listed within the algorithm under Comprehensive Geriatric Assessment. Potential interventions recommended by the panel include referral to physical medicine and rehabilitation (PM&R) and/or occupational therapy (OT) and/or a geriatric-trained clinician or a primary care physician, a home safety evaluation, and the promotion of physical activity and exercise.

### Comorbidities

Older adults have an increased prevalence of comorbidities that may impact cancer prognosis and treatment tolerance.<sup>79,80</sup> Cardiovascular problems including congestive heart failure (CHF), coronary artery disease

(CAD), diabetes mellitus, renal insufficiency, dementia, depression, anemia, chronic infections, neuropathy, anemia, liver and lung disease, hearing or vision loss, osteoporosis, decubitus or pressure ulcers, and prior cancer diagnosis and treatment are some of the frequently encountered comorbid conditions in older patients with cancer.

Specific comorbidities have been shown to have an impact on prognosis and treatment outcomes in patients with cancer.<sup>81-83</sup> In a randomized adjuvant chemotherapy trial of 3759 patients with high-risk stage II and stage III colon cancer, patients with diabetes mellitus experienced a significantly higher rate of overall mortality and cancer recurrence. At 5 years, the disease-free survival (DFS; 48% vs. 59%), OS (57% vs. 66%), and relapse-free survival (RFS; 56% vs. 64%) were significantly worse for patients with diabetes compared with patients without diabetes.<sup>81</sup> In another series of 5077 patients (median age, 69.5 years) with localized or locally advanced prostate cancer, neoadjuvant hormonal therapy was significantly associated with an increased risk of all-cause mortality (26.3% vs. 11.2%) among patients with a history of CAD, CHF, or myocardial infarction after a median follow-up of 5.1 years.<sup>82</sup> In the SEER-Medicare database analysis of older patients ( $\geq 66$  years) diagnosed with stages I–III breast cancer, those with diabetes had an increased rate of hospitalizations for any chemotherapy toxicity and higher all-cause mortality.<sup>83</sup>

The interaction of cancer treatment with comorbidities may impact functional status or worsen the comorbidity. Cancer-specific treatment may be overly risky due to the type and severity of the comorbidity. For example, chronic lung disease may affect the ability to perform thoracic surgery, or administer RT to the lungs, and extensive cardiac disease will limit the use of potential cardiotoxic drugs. Renal function carries significant weight when determining treatment approach as many of the chemotherapy agents are excreted by the kidneys, and dose



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adjustments to the measured glomerular filtration rate (GFR) should be considered since the GFR decreases with age. Furthermore, comorbidity may influence life expectancy (independent of cancer), thus affecting treatment recommendations. The effect of comorbidity on life expectancy should be evaluated prior to the initiation of treatment.

The Charlson Comorbidity Index (CCI),<sup>84</sup> Cumulative Illness Rating Scale for Geriatrics (CIRS-G),<sup>85</sup> Older Americans Resources and Services (OARS) Questionnaire,<sup>86,87</sup> and Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI)<sup>88</sup> are commonly used to determine the risk of mortality associated with comorbidity in older patients. CCI<sup>89</sup> and CIRS-G<sup>90,91</sup> have also been used to determine treatment tolerance in older patients with cancer. In a study of 310 older patients ( $\geq 70$  years) with head and neck cancer, comorbidity as measured by the ACE-27 index was an indicator of OS.<sup>92</sup> In a randomized trial that compared vinorelbine alone or in combination with gemcitabine in older patients with locally advanced non-small cell lung cancer (NSCLC), a CCI of greater than 2 was associated with a higher risk of early treatment cessation (82% vs. 30%, respectively).<sup>89</sup> In a phase III trial comparing platinum-doublet therapy as first-line treatment in patients with advanced-stage NSCLC, patients with severe comorbidities (as measured by CIRS-G) benefited from and tolerated platinum-doublet chemotherapy as well as patients with no comorbidities.<sup>90</sup> However, the former group had a higher risk of neutropenic fever and death from neutropenic infections. The OARS questionnaire assesses the presence of 13 common comorbidities and additionally inquires about the degree to which the individual comorbid conditions interfere with daily activities.<sup>87</sup> In a study including 539 older patients, 92% reported 1 or more comorbid conditions using the patient-reported OARS questionnaire, with arthritis and hypertension being the most prevalent, and 62% reported functional limitation due to comorbidity. Another study evaluated the association between comorbidity, toxicity, time to relapse, and OS in older patients with good performance status

receiving adjuvant chemotherapy for early-stage breast cancer using OARS. In these patients, comorbidity was associated with shorter OS, but was not associated with increased treatment-related toxicity or relapse.<sup>86</sup>

Finally, in a retrospective cohort study of patients aged 50 years and older who had undergone allogenic HCT, high HCT-CI score ( $\geq 3$ ) was found to be more predictive than age, conditioning intensity, or performance status for a lower OS (HR, 2.2;  $P = .02$ ). Adverse events (grade 3–4) following HCT were also more common in patients with high HCT-CI ( $P = .02$ ).<sup>93</sup> It is recommended that for older adults with comorbidities, clinicians optimize each medical condition prior to therapy, evaluate the patient's life expectancy, and coordinate with the patient's primary care physician and team of specialists.

### Social Functioning and Support

The availability of social support has been associated with physical health and emotional well-being of patients with cancer.<sup>94</sup> Older adults with cancer require dependable social support systems to optimize treatment outcomes. Additionally, the lack of social ties has been identified as a significant predictor of mortality in older adults.<sup>94,95</sup> Therefore, providers should conduct a comprehensive evaluation of the older adult's social support system prior to starting anti-cancer therapy. The patient's living conditions, presence, and adequacy of caregiver and financial status should be considered. Information should be sought as to whether the patient is a caregiver for someone else and whether cancer treatment may impact their ability to provide this care. Finally, the patient's treatment goals should be discussed, clarifying advance directives and the presence of a health care proxy.

The self-administered, 19-item Medical Outcomes Study (MOS) social support survey measures the availability of support in several domains using four subscales (ie, emotional/informational, tangible/instrumental,



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positive social interaction, affection) and one overarching index.<sup>96,97</sup> To facilitate its administration, the survey has been abridged to a modified, eight-item survey with two subscales, encompassing two domains of social support (emotional and tangible).<sup>96</sup> In an analysis of 3241 patients who completed either the MOS social support survey or the modified MOS social support survey, the results of the modified survey were found to be comparable to that of the MOS social support survey.<sup>96</sup> Other assessment tools include the RAND Health Care Social Support Survey Instrument: Emotional/Informational Subscale and the RAND Health Care Social Support Survey: Tangible Subscale.

In the case of deficient social support, the NCCN Older Adult Oncology Panel recommends several potential interventions, including referral to social work for a thorough evaluation, home safety review and issue of medical alert devices, psychiatry/psychology consultation, spiritual care, and screening for elder abuse and caregiver burden.

### Cognition

Older patients with cancer who are cognitively impaired have an increased risk of functional dependence, a higher incidence of depression, and a greater risk of death. Cognitive function is also predictive of medication nonadherence across diagnoses, regardless of the complexity of regimen.<sup>98</sup> Cognitively impaired patients should be cared for by an experienced multidisciplinary geriatric oncology team along with good supportive care throughout treatment.<sup>99</sup> In addition, the association between cognitive impairment and the ability to weigh the risks and benefits of cancer treatment decisions needs to be considered.

Often present in older patients as a comorbid condition, dementia is a progressive condition characterized by impairment of memory and at least one other cognitive function (such as aphasia, apraxia, agnosia, or executive function) that would interfere with the ability to perform daily

functions independently. Mild cognitive impairment is an intermediate state between normal cognition and dementia. It is characterized by subjective memory impairment, preserved general cognitive function, and intact ability to perform daily functions.<sup>100</sup> Clinical interview with cognitive and functional assessment to screen for mild cognitive impairment or dementia is recommended for all patients, since there is a strong correlation between decline in cognitive status and the loss of functional independence in older adults.<sup>101</sup>

The MMSE is recommended for the assessment of cognitive function in older adults.<sup>102-105</sup> MMSE is an 11-item screening test that quantitatively assesses the severity of cognitive impairment and documents cognitive changes occurring over a period of time.<sup>103,104</sup> However, MMSE is not adequate for mild cognitive impairment and does not predict future decline.

The Guidelines also include the Mini-Cog as a screening tool for the assessment of mild cognitive impairment and dementia in older patients with cancer. Mini-Cog is a 5-point test (consisting of a three-word recall and clock drawing test) used for screening cognitive impairment in the older population.<sup>106,107</sup> Finally, the Blessed Orientation Memory Concentration Test (BOMC) is also included in the Guidelines. The BOMC is a weighted, six-item survey that evaluates patients' orientation, registration, and attention in order to diagnose dementia.<sup>108</sup>

Assessment of cognitive function can also be confounded by fatigue, depression, anxiety, underlying cerebral disease, endocrine dysfunction, nutritional deficiency, alcohol use, and sleep disturbances.<sup>109</sup> Therefore, if dementia is suspected, further evaluation including brain imaging, neuropsychological testing, and evaluation for vitamin B12 deficiency and thyroid dysfunction may be indicated. The use of certain classes of medications (anticholinergics, antipsychotics, benzodiazepines, corticosteroids, and opioids) has been associated with cognitive



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impairment and delirium in older adults.<sup>110-112</sup> Antipsychotic drugs are also associated with higher mortality rates in patients with dementia.<sup>113-115</sup> Research suggests that chemotherapy is also responsible for cancer-related cognitive decline. Chemotherapy-related cognitive impairment may persist for months to years following treatment and the reasons are varied. Hilmer and colleagues developed a drug burden index, which is a useful evidence-based tool for assessing the effect of medications on physical and cognitive performance in older adults.<sup>116</sup> Special considerations for over- or under-use, duration of therapy, and dosage should be in place with the use of these classes of medications.

For patients with suspected impaired cognitive function that may potentially interfere with their decision-making capacity, the Guidelines recommend consultation with a clinician experienced in cognitive evaluation (geriatric-trained clinician, neurologist, geriatric psychiatrist, or neuropsychologist) for initiation of further evaluation to determine the appropriate diagnosis (eg, mild cognitive impairment, dementia, delirium).<sup>117</sup> In addition to the clinical observation by the medical team, any concerns reported by the patient or the patient's family suggestive of impaired cognitive function should also trigger further evaluation. The NCCN Guidelines recommend periodic reassessment of cognitive function, especially when considering changes to treatment plan for all patients, including those with no cognitive impairment.

### Psychological

Depression and distress have been identified in about 28% and 41% of older adults with cancer, respectively, and their prevalence can have a significant impact on a patient's ability to receive treatment for his/her cancer.<sup>118,119</sup> Impaired mobility and functional status, impaired ADL, inadequate social support, cognitive impairment, polypharmacy, multimorbidity, and cancer-related pain were independently associated with clinical depression, whereas poorer physical function and loss of

independence were the key risk factors contributing to distress.<sup>118,119</sup> Beauplet and colleagues highlight the lack of evidence-based knowledge in evaluating depression in older adult patients with cancer leading to difficulty in guiding the treatment approach in this setting, and stress that psycho-oncologic evaluation through screening tests is a must along with intervention from a trained geriatric clinician.<sup>120</sup>

To screen for depression, the Geriatric Depression Scale (GDS) is a reliable and valid tool for older patients with no or moderate cognitive impairment.<sup>121</sup> GDS was originally developed as a 30-item scale.<sup>121</sup> Shortened versions of GDS have been found to be equally accurate and less time consuming in screening for depression in older adults.<sup>122,123</sup> Cancer-related fatigue and depression frequently occur together; therefore, patients reporting fatigue could benefit from an assessment for depression.<sup>124-126</sup>

In the prospective ELCAPA cohort study, the overall prevalence of clinical depression was 28% among older patients with cancer that had not yet been treated.<sup>118</sup> In a multivariate analysis, geriatric assessment findings including impaired mobility and functional status, ADLs, inadequate social support, cognitive impairment, polypharmacy, multimorbidity, and cancer-related pain were independently associated with clinical depression.

The Patient Health Questionnaire (PHQ-2 and PHQ-9) is also used as a tool to evaluate for depression in older patients with cancer. PHQ-2 consists of the first two items of PHQ-9, and is a brief screening tool administered prior to the longer questionnaire PHQ-9. In an individual participant data meta-analysis of 10,627 patients, the PHQ-2/PHQ-9 combination had a sensitivity of 82%, specificity of 87%, and area under the receiver operating characteristic (ROC) curve of 0.90.<sup>127</sup>

Similarly, psychological distress is common among patients with cancer. Hurria and colleagues reported that significant distress was identified in



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41% of patients 65 years and older with cancer, and poorer physical function was the best predictor of distress.<sup>119</sup> Screening tools have been found to be effective and feasible in reliably identifying distress and the psychosocial needs of patients.<sup>128-130</sup> The NCCN Distress Thermometer (DT) and the accompanying 36-item Problem List is a well-known screening tool, specifically developed for patients with cancer by the NCCN Distress Management Panel.<sup>131,132</sup> The NCCN DT has been validated by several studies in patients with different types of cancer and has revealed good correlation with the more comprehensive Hospital Anxiety and Depression Scale.<sup>130</sup> Patients can quickly fill out this distress assessment tool in the waiting room and the tool can alert the physician to potential problems. This tool identifies whether patients with cancer have problems in five different categories: practical, family, emotional, spiritual/religious, and physical. See the NCCN Guidelines for Distress Management for more information on the use of DT as a screening tool in patients with cancer.

Finally, the Mental Health Inventory (MHI-17) is a method to evaluate overall emotional functioning by measuring the level of depression and anxiety experienced within the past month. For those detected to have psychological impairment, potential interventions are listed within the algorithm under *Comprehensive Geriatric Assessment*.

### Nutrition

Nutritional deficiency or malnutrition is a common and serious condition that is underdiagnosed in older patients with cancer. Poor nutritional status is associated with an increased risk of severe hematologic toxicity, an increased mortality risk, poor chemotherapy tolerance, and an increased length of stay among hospitalized patients with cancer.<sup>133-136</sup> While some of the malnutrition is attributed to the underlying illness, in most of the patients it is due to inadequate intake of calories. Nutritional parameters would help to identify patients for individualized or advanced

intervention. There are many scales for nutritional assessment and no clear data to identify the most sensitive scale. A meta-analysis evaluated the ability of 15 markers of nutritional status to predict patient outcomes and concluded that no single screening tool can distinctly identify malnutrition due to lack of uptake/intake of food from inflammatory causes of weight loss.<sup>137</sup> The malnutrition universal screening tool uses cutoffs such as a body mass index (BMI) of less than or equal to 22 kg/m<sup>2</sup> and percent of unintentional weight loss of greater than 5% over 6 months.<sup>138</sup>

The Mini Nutritional Assessment (MNA) is a validated, self-reported tool that can identify older adults who are malnourished or at risk for malnutrition. The summated scores differentiate between those with sufficient nutrition, with protein-calorie malnutrition, or who are at risk of malnutrition. Finally when evaluating patients for potential nutritional deficits, special attention should also be devoted to vitamin D deficiency since that may be related to osteoporosis and fractures.<sup>139</sup>

For those detected to have nutritional deficits, the NCCN Older Adult Oncology Panel recommends a nutrition consult, specific dietary interventions, oral care, supplemental nutrition, OT for assistive devices, speech therapy and swallowing assessment, oral/dental evaluation for dentures, screening for food insecurity, social/caregiver support, and evaluation for appetite stimulants, nausea control, and calorie, protein, and fluid recommendations.

### Polypharmacy

Polypharmacy can be defined in various ways, including the use of increased number of medications ( $\geq 5$ , more than is clinically indicated); the use of potentially inappropriate medications; medication underuse; and medication duplication.<sup>140</sup> Although polypharmacy can be an issue across all age groups, it can be more prevalent and pose a serious problem for older patients due to the presence of increased comorbid conditions treated with multiple drugs. The use of cancer therapy as well as



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medications for management of treatment-related symptoms or side effects can result in polypharmacy.<sup>141-143</sup>

The use of multiple medications can lead to increased incidences of adverse drug reactions, which can lead to functional decline, other geriatric syndromes, and non-adherence.<sup>144,145</sup> Among patients with cancer receiving systemic anticancer therapy for solid tumors, one or more drug-drug interactions were observed in 27% of patients, which increased to 31% among patients with cancer receiving palliative care only.<sup>146</sup> Older patients and those with comorbid conditions are at greater risk of drug interactions.<sup>146</sup>

Alterations in pharmacokinetics and pharmacodynamics of drug metabolism in the older population can also contribute to adverse drug interactions.<sup>147</sup> Most of the commonly prescribed medications such as opioids, antidepressants, antibiotics, and antipsychotics as well as anticancer drugs induce or inhibit cytochrome P-450 enzymes. In a retrospective analysis of 244 older patients ( $\geq 70$  years), Popa and colleagues assessed the impact of potential drug interactions (PDIs) and their association with chemotherapy tolerance.<sup>148</sup> The results of this study demonstrated that PDIs may contribute to severe non-hematologic toxicities, whereas there was no association between PDIs and hematologic toxicities. Further research regarding PDIs and anti-cancer therapy toxicity is warranted in order to develop interventions and optimize clinical outcomes in older patients receiving these treatments.

The use of one or more potentially inappropriate medications among older patients has also been documented in several studies.<sup>149-151</sup> In one study, the use of inappropriate medications increased from 29% to 48% among patients with cancer in the palliative care setting.<sup>150</sup> In a study of 500 older patients with cancer ( $\geq 65$  years) starting a new chemotherapy regimen, polypharmacy ( $\geq 4$  drugs) was observed in over 60% of patients and the use of potentially inappropriate medications was commonly seen in less

than or equal to 29% of patients. Polypharmacy did not increase the risk of chemotherapy-related toxicity in this cohort, frequency of hospitalization, or early discontinuation of chemotherapy.<sup>151</sup> The use of potentially inappropriate medications (especially hypnotics, sedatives, antidepressants, long-acting benzodiazepines, other psychotropics, and medications with anticholinergic properties) is also associated with an increased risk of falls in older adults ( $\geq 65$  years).<sup>152,153</sup>

### *Evaluation of Polypharmacy*

The Guidelines recommend evaluation of adherence to therapy and periodic medication review to check for medication duplication, appropriate use, availability of less expensive alternative medications, and PDIs. The panel also recommends the careful evaluation of the use of supplements and herbal therapies. Although the optimal polypharmacy cut-point for predicting clinically important adverse events in older people with cancer is unclear, the common definition of 5 or more medications is reasonable for identifying patients for medication review.<sup>154</sup> Medication review of existing prescription and over-the-counter medications may be indicated prior to initiation or change in treatment, change in comorbid disease management or in clinical condition, and at other times as determined by the clinical team and during transition of care. A careful review of the indication for treatment, duration of therapy, and dosage should be performed when using specific medications or classes of medications that are not recommended for older adults. See the section on *Medications Commonly Used for Supportive Care that are of Concern in Older Patients* in the algorithm for specific recommendations.

Beers Criteria and the Medication Appropriateness Index (MAI) are two of the most common approaches used to evaluate potentially inappropriate medication use in older patients. The Screening Tool of Older Persons' Prescriptions (STOPP) and the Screening Tool to Alert doctors to Right



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Treatment (START) criteria have been developed to evaluate drug interactions, medication duplication, and medication underuse.

### *Beers Criteria*

The Beers Criteria identify inappropriate medications that have potential risks that outweigh potential benefits based on the risk of toxicity and the presence of potential drug-disease interaction in older patients with cancer.<sup>155,156</sup> The criteria are appropriate for persons older than 65 years of age and provide a rating of severity for adverse outcomes as well as a descriptive summary of the prescribing information associated with the medication. The updated Beers Criteria have been used to evaluate polypharmacy in older patients with cancer both in an oncology-specific acute care unit (Oncology-Acute Care for Elders [OACE]; n = 47 with a median age of 73.5 years) and in the outpatient setting (n = 154 with a median age of 74 years).<sup>157,158</sup> The Beers Criteria-based polypharmacy was observed in 21% and 11% of patients, respectively. Both of these studies had implemented medication review and pharmacist-based interventions to improve the appropriateness of prescribing. In the OACE study, 53% had a subsequent alteration in their medication regimen and 28% had a potentially inappropriate medication discontinued, after implementation of recommendation by the OACE team.<sup>157</sup> In the outpatient study, 50% of patients required specific interventions and the use of potentially inappropriate medication was identified in 11% of patients, following geriatric management evaluation.<sup>158</sup>

The Beers Criteria were updated by the American Geriatrics Society (AGS) to improve monitoring of drug use, e-prescribing, interventions to decrease adverse events in older adults, and patient outcomes.<sup>159</sup> In the updated criteria, medications that are used in older adults are divided into: medications that should be avoided in most older patients, medications that should be avoided in older patients with select conditions, medications that should be administered with caution as the benefits outweigh the

risks, medication interactions, and dose adjustment of medication based on renal function.<sup>160</sup>

### *Medication Appropriateness Index*

MAI was developed to measure appropriate prescribing based on a 10-item list and a 3-point rating scale.<sup>161</sup> Samsa and colleagues subsequently modified the MAI to include a single summated MAI score per medication that demonstrated acceptable reliability in assessing medication appropriateness among 1644 medications prescribed to 208 older veterans from the same clinic.<sup>162</sup> This modified MAI appears to be a valid and relatively reliable measure to detect medication appropriateness and inappropriateness in the community pharmacy setting as well as in ambulatory older patients on multiple medications.<sup>163,164</sup> MAI scores were significantly lower for medications with a high potential for adverse effects compared with those with a low potential (1.8 vs. 2.9;  $P < .001$ ).<sup>163</sup> Higher MAI scores were also associated with lower self-related health scores in older adults.<sup>165</sup> MAI has not been evaluated extensively in older patients with cancer.

### *STOPP/START Criteria*

STOPP/START criteria were established using the Delphi consensus and an 18-member expert panel from the academic centers of Ireland and the United Kingdom.<sup>166</sup> The STOPP criteria are comprised of 65 indicators for potentially inappropriate prescribing, including drug-drug and drug-disease interactions, therapeutic duplication, and drugs that increase the risks of geriatric syndromes, whereas the START criteria incorporate 22 evidence-based indicators to identify prescribing omissions in older people.<sup>167,168</sup> In a randomized trial of 400 hospitalized patients ( $\geq 65$  years), unnecessary polypharmacy, the use of drugs at incorrect doses, and potential drug-drug and drug-disease interactions were significantly lower in the group assigned to screening with STOPP/START criteria with recommendations provided to their attending physicians compared to the



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control group assigned to routine pharmaceutical care.<sup>169</sup> Significant improvements in prescribing appropriateness were sustained for 6 months after discharge.

### Geriatic Syndromes

Falls, dementia, delirium, depression, distress, osteoporosis, fatigue, and frailty are some of the most common syndromes in older patients with cancer.<sup>170</sup> Older patients with cancer experience a higher prevalence of geriatric syndromes than those without cancer. In an analysis of a national sample of 12,480 community-based elders, 60.3% of patients with cancer reported one or more geriatric syndromes compared with 53.2% of those without cancer.<sup>171</sup> In this cohort, the prevalence of hearing trouble, urinary incontinence, depression, and osteoporosis were significantly higher among those with cancer.

### Fatigue

Cancer-related fatigue is a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning.<sup>172</sup> In advanced cancer, the prevalence of fatigue is greater than 50% to 70%.<sup>173</sup> In a study that evaluated the prevalence of common symptoms in patients with advanced cancer, fatigue was independently associated with chemotherapy, hemoglobin level, and other symptoms such as pain and depression.<sup>174</sup> Patients perceive fatigue to be one of the most distressing symptoms associated with cancer and its treatment, more than pain or nausea and vomiting.<sup>175,176</sup> In contrast to normal fatigue, cancer-related fatigue is refractory to sleep and rest, perhaps because patients with cancer have aberrant sleep patterns. It is reasonable to expect that fatigue may precipitate functional dependence, especially in patients who are already dependent in IADLs.<sup>70,177,178</sup>

Multiple factors can contribute to fatigue, including pain, emotional distress, anemia, comorbidities, medications, and/or sleep disturbance;

many of them are treatable. Certainly, the best strategy is avoidance of any fatigue that may precipitate functional dependence in older adults. Energy conservation, exercise programs, stress management, sleep therapy, and psychostimulants are some of the interventions that have proved valuable. Screening for fatigue can be done using a brief screening questionnaire that would enable patients to rate the severity of their fatigue on a scale of 0 (no fatigue) to 10 (worst fatigue). See the NCCN Guidelines for Cancer-Related Fatigue available at [www.NCCN.org](http://www.NCCN.org).

### Frailty

Frailty is a biologic syndrome of decreased reserve and resistance to stressors, causing vulnerability to adverse outcomes.<sup>179</sup> Frail patients are at risk for falling, disability, hospitalization, and death. Fried Frailty Criteria and the Balducci Frailty Criteria are the two most common measures used to identify frail patients.<sup>22,48</sup> A study showed that very few patients were classified as frail based on the oncologist's clinical judgment, and the use of a geriatric assessment can aid the oncologists to better identify frail patients.<sup>180</sup>

According to Fried Frailty Criteria, frailty is defined as a clinical syndrome with three or more of the following conditions: unintentional weight loss ( $\geq 10$  lb in the past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and/or low physical activity.<sup>48</sup> In a prospective, observational study of 5317 patients ( $\geq 65$  years), frailty status based on these criteria was found to be predictive of incident falls, worsening mobility or ADL function, incidence of hospitalization, and death.<sup>48</sup>

The Balducci Frailty Criteria are based on the components of CGA (dependence in one or more ADLs, three or more comorbid conditions, and one or more geriatric syndromes).<sup>22</sup> These CGA-frailty criteria have been found to be more useful in identifying frail patients with cancer. In a prospective study that compared the Balducci Frailty Criteria and the



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modified version of Fried Frailty Criteria in 176 patients (aged 70–94 years) who underwent elective surgery for CRC, although both frailty measures were predictive of OS, the Balducci Frailty Criteria were more useful than the modified version of the Fried Frailty Criteria in predicting postoperative complications.<sup>181</sup>

### Osteoporosis

Osteoporosis and its associated increased risk of fracture is a major risk factor in patients with cancer, especially in patients receiving chemotherapy or hormonal therapy for breast cancer and in patients receiving hormonal therapy for prostate cancer. Osteoporosis can be prevented with appropriate screening, lifestyle interventions, and therapy. The diagnosis of osteoporosis is based on assessment of bone density by a dual-energy x-ray absorptiometry (DEXA) scan.

Management of bone health has become an integral part of comprehensive cancer care. Older patients should be made aware of the impact of cancer therapies on bone health and should adhere to treatment recommendations for maintaining bone health.<sup>182</sup> The NCCN Task Force Report on Bone Health in Cancer Care discusses effective screening and therapeutic options for optimizing bone health in patients with cancer.<sup>183</sup>

### Falls

Falls are more common in older adults with a cancer diagnosis than those without cancer. Cancer diagnosis (especially in the first 6 months after diagnosis) and chemotherapy are also associated with a high risk of falls.<sup>184–186</sup> In a prospective study of 185 patients with advanced cancer, 93 (50.3%) patients experienced falls associated with a high risk of physical injury, regardless of age: 35 patients were older than 65 years of age and 58 patients were 65 years of age or older.<sup>184</sup> The median time to a fall was 96 days. In a multivariate analysis, the diagnosis of a primary brain tumor or brain metastasis, number of falls in the preceding 3 months, severity of depression, benzodiazepine dose, and cancer-related pain were identified

as independent risk factors.<sup>184</sup> Another study also reported that the risk of falls increases with each cycle of chemotherapy, and patients treated with taxane-based chemotherapy may be at a greater risk of falls than those treated with platinum-based chemotherapy.<sup>185</sup> In a study that evaluated the occurrence of falls in 937 older adults with cancer, during the follow-up of 2 to 3 months after cancer treatment decision, a fall was reported by 142 patients (17.6%), of whom 51.4% fell more than once. Fall history in the past 12 months, fatigue, ADL dependency, geriatric risk profile by G8, and living alone were identified as independent predictors of 1 or fewer falls within 2 to 3 months after cancer treatment decision.<sup>187</sup> In addition, there are some data indicating the impact of falls in the interruption or cessation of subsequent cancer treatment.<sup>188</sup> These findings suggest that falls are important problems in older patients with cancer and that geriatric assessment can identify patients at risk for falls.

Multifactorial risk assessment and management, exercise, vitamin D supplementation, withdrawal of psychotropic medications, and environmental modifications have been shown to be effective in reducing the risk and/or rate of falls in older patients.<sup>189–194</sup> The Guidelines recommend periodic assessment of history of falls, balance, and gait difficulties for all patients, as fall risk may change over time. The use of early and preventative use of durable medical equipment and in-home safety evaluations are recommended for patients with neurotoxicities at high risk for falls. Assessment of gait by evaluating gait speed<sup>15</sup> or using the TUG test, evaluation for physical therapy or OT, vitamin D supplementation (in patients with low levels of vitamin D), or referral to geriatrics or a primary care physician can be considered for patients who have experienced a fall in the last 6 months or if they are afraid of falling. Finally, risk of falls should be considered carefully when making treatment decisions, as prescribing medications that can induce peripheral neuropathy may significantly increase this risk.



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### *Delirium*

Delirium is an acute decline in attention and cognition developed over a short period of time (usually hours to days) and is characterized by disturbance of consciousness with reduced ability to focus, sustain, or shift attention.<sup>195</sup> It is a common, serious, costly, under-recognized and easily overlooked problem in older adults that can contribute to complications such as poorer clinical outcomes, functional decline, impaired communication between the patient and physicians, longer length of hospital stay, and death.<sup>196</sup> Dementia is the leading risk factor for delirium and about two thirds of cases of delirium occur in older patients with dementia.<sup>195</sup>

Many other predisposing factors such as vision or hearing impairment, history of alcohol abuse, functional dependency, and multiple comorbidities were consistently identified across patient populations.<sup>195</sup> Precipitating factors such as polypharmacy, dehydration, use of psychoactive drugs, and physical restraints can lead to delirium. Predictive models for delirium can be useful in identification as well as stratification of risks of delirium to assist health care providers in implementing preventive measures and improve outcomes.<sup>195</sup>

With respect to older patients with cancer, cognitive dysfunction is one of the most common direct effects of primary and secondary CNS tumors (brain or meningeal metastasis). Para-neoplastic neurologic syndromes are potential causes of delirium. Toxicities from cancer-specific treatment with radiation, chemotherapy, and immunotherapy as well as supportive medications such as antihistamines, antiemetics, and anxiolytics also can lead to delirium and cognitive impairment.<sup>197,198</sup>

The Confusion Assessment Method (CAM) is the most utilized screening and diagnostic tool based on four important features of delirium: acute onset and fluctuating course, inattention, disorganized thinking, and altered level of consciousness.<sup>199,200</sup> The Memorial Delirium Assessment

Scale is a 10-item validated instrument developed for repeated use to quantify the severity of delirium symptoms in patients with advanced cancer.<sup>201</sup> The Nursing Delirium Screening Scale is an observational 5-item scale and has been validated in the oncology inpatient setting and is associated with high sensitivity and specificity.<sup>202</sup>

The NCCN Guidelines have included CAM as a screening tool for delirium. Delirium is usually multifactorial. A complete evaluation and treatment of all potential causes of delirium is recommended for all patients with delirium, including conducting a thorough medication review and deprescribing agents that can contribute to delirium such as psychoactive medications and narcotics.<sup>203-205</sup> Other potential contributing factors such as sleep deprivation, immobility, visual and hearing impairment, malnutrition, and dehydration should be addressed and non-pharmacologic approaches should be used. Pharmacologic interventions should be reserved for patients with severe agitation, which could result in interruption of essential medical therapies or could pose a danger for self-injury, or for those with distressing psychotic symptoms (eg, hallucinations, delusions).<sup>195</sup>

### **Considerations for Older Adults Undergoing Cancer-Specific Treatment**

#### **Surgery**

In general, age is not the primary consideration for surgical risk, although the physiologic status of the patient needs to be assessed.<sup>206</sup> All older adults undergoing surgery should undergo an assessment for components of frailty, including comorbidities, mobility, functional status, and nutrition.<sup>207</sup> The American College of Surgeons (ACS) Geriatric Surgery Verification (GSV) program provides a framework for hospitals to take an interdisciplinary approach to continuously optimize surgical care of older adults. The GSV program includes 30 standards to improve surgical care for older adults with an emphasis on goals of care and shared decision-



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making, assessment of geriatric-specific vulnerabilities (eg, cognition, mobility), and interdisciplinary postoperative care.<sup>205</sup> The ACS National Surgical Quality Improvement Program Surgical Risk Calculator includes both geriatric-specific predictors and geriatric-specific outcomes; the ACS Surgical Risk Calculator can be a useful tool for sharing patient-specific predicted outcomes after surgery and facilitating a more informed discussion regarding risks of surgery.<sup>208</sup> The tool's functionality was enhanced by collecting data from more than 38,000 older patients and comparing performance in outcomes prediction using the traditional ACS Surgical Risk Calculator with models that also included geriatric risk factors.

Older age is also a risk factor for postoperative delirium, which is the most common postoperative complication in older adults. About 40% of the delirium in older patients is preventable, which makes it a prime candidate for prevention interventions targeted to improve the outcome of older adults after surgery.<sup>209,210</sup> The AGS practice guidelines have presented both nonpharmacologic and pharmacologic interventions for prevention and treatment of postoperative delirium in older adults. The guidelines cover the topic areas of delirium risk factors, diagnosis and screening, prevention, medical evaluation, and pharmacologic treatment.<sup>209</sup>

### Radiation Therapy

RT (external beam RT [EBRT] or brachytherapy) can be offered either in the curative or palliative setting.<sup>211,212</sup> Available data from the literature indicate that RT can be highly effective and well tolerated, so that age alone need not be a limiting factor in older patients with cancer.<sup>213,214</sup> Radiation oncologists, like all other clinicians caring for older patients with cancer, must be careful of the potential to overtreat older adults with substantial competing risks of non-cancer death, as well as the potential to undertreat older adults because of an underestimation of life expectancy in patients with advanced age but few significant comorbid conditions.

It is important to consider several general principles when developing an individualized treatment plan with RT in older patients.<sup>212</sup> The decision to offer RT to older patients with cancer should be based on the following factors: 1) evaluation of the benefits and risks associated with RT; 2) careful consideration of the patient's underlying functional reserve; and 3) an understanding of the differences in the biology of cancers and their responsiveness to therapy in this patient population. Since the biologic characteristics of certain cancers are different in older patients compared to their younger counterparts, and partly because of the decreased tolerance of treatment by older patients, treatment should be individualized based on the nature of the disease and the performance status of the patient. Nutritional support and pain control for treatment-induced mucositis are recommended for patients receiving RT. Considerations for older patients undergoing RT will heavily depend on the anatomic site being radiated and the dose/fractionation chosen. See disease-specific NCCN Guidelines for Treatment by Cancer Type available at [www.NCCN.org](http://www.NCCN.org). Concurrent chemoradiation, however, should be used with caution; dose modification of chemotherapy may be necessary to reduce toxic side effects.

Incomplete and interrupted courses of RT can compromise the efficacy of treatment as well as the ability to deliver higher doses of RT in the future. Therefore, it is important to consider alternative approaches in patients with extreme functional limitations and ensure maximal supportive care. Advanced RT techniques (eg, intensity-modulated RT [IMRT], image-guided RT [IGRT], and stereotactic body RT [SBRT] or stereotactic ablative radiotherapy [SABR]) facilitate the delivery of large doses of radiation to small target volumes while limiting the risk of radiation-induced damage to normal surrounding tissues and organs at risk (OARs).<sup>214</sup> Judicious application of these techniques may also help to assuage concerns about the risks of RT in older adults. Hypofractionated RT may



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also help to improve treatment tolerability by limiting overall treatment time without compromising clinical outcomes in some patients.<sup>215</sup>

RT, though administered locally, can produce systemic side effects such as fatigue, depression, anorexia, nausea, vomiting, alteration in taste, sleep disturbance, headache, anemia, dry skin, dermatitis, and constipation. Late complications of these therapies also include pharyngitis, esophagitis, laryngitis, persistent dysphagia, fatigue, cardiovascular disease, mucositis, hepatotoxicity, and cognitive deficits.<sup>216,217</sup>

### Systemic Therapy

Several retrospective studies have reported that the toxicity of chemotherapy is not more severe or prolonged in persons older than 70 years of age.<sup>218-221</sup> However, the results of these studies cannot be generalized for the following reasons:

- Only a few patients were 80 years of age or older; therefore, minimal information is available on the oldest patients.
- The older patients involved in these studies were highly selected by the eligibility criteria of the cooperative group protocols and were not representative of the general older population, because they were probably healthier than most older patients.
- Many of the treatment regimens used in these trials had lower dose intensity than those in current use.

Nevertheless, these studies are important, because they demonstrate that age, by itself, is not a contraindication to cancer therapy. Therefore, patient selection is extremely important to maximize the benefits of systemic therapy in older patients with cancer.

More studies have emerged studying impact of chemotherapy on older cancer patients. For example, cognitive functioning (assessed through MMSE) was not worst among breast cancer patients aged 70 to 80 years treated with immunotherapy with chemotherapy combination as compared to those treated with immunotherapy alone.<sup>222</sup> In another retrospective evaluation of NSCLC patients aged 85 years or more, epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) as first-line therapy showed greater benefit than cytotoxic chemotherapy or best supportive care alone with OS of 16.9, 7.2, and 9.8 months, respectively.<sup>223</sup>

Increased age has been associated with changes in the pharmacokinetics and pharmacodynamics of cancer therapy and increased susceptibility of normal tissues to toxic complications.<sup>224</sup> Pharmacodynamic changes of interest include reduced repair of DNA damage and increased risk of toxicity. Pharmacokinetic changes of major concern include decrease in the GFR and volume of distribution of hydrosoluble drugs. Although the hepatic uptake of drugs and the activity of cytochrome P450 enzymes also decrease with age, the influence of these changes on cancer chemotherapy is not clear. Intestinal absorption may decrease with age, but it does not appear to affect the bioavailability of anticancer agents. The pharmacokinetics of antineoplastic drugs is unpredictable to some extent; thus, drug doses should be adjusted according to the degree of toxicity that develops. However, adequate dosing is necessary to ensure the effectiveness of therapy.

Extermann and colleagues have devised the MAX2 index for estimating the average per-patient risk for toxicity from chemotherapy.<sup>225</sup> In a retrospective analysis, Shayne et al identified advanced age ( $\geq 65$  years), greater body surface area, comorbidities, anthracycline-based regimens, a 28-day schedule, and febrile neutropenia as independent predictors of reduced dose intensity among patients with early-stage breast cancer receiving adjuvant chemotherapy.<sup>226</sup> In another retrospective analysis of



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older patients ( $\geq 65$  years) with invasive breast cancer, the type of adjuvant chemotherapy regimen was a better predictor of toxicity than increased age or comorbidity score.<sup>227</sup> Anthracycline-based regimen resulted in greater grade 3 or 4 toxicity, hospitalization, and/or febrile neutropenia, whereas treatment delays due to myelosuppression were more frequent with the cyclophosphamide-containing regimen. Among older patients with ovarian cancer, those receiving standard-dose chemotherapy were more likely to experience cumulative toxicity and delays in therapy versus those receiving reduced-dose intravenous carboplatin/paclitaxel.<sup>228</sup>

Other investigators have developed tools incorporating components of CGA to assess the individual risk of severe toxicity from chemotherapy in older patients.<sup>59-61</sup> Hurria and colleagues have developed a cancer-specific geriatric assessment (CSGA) for predicting treatment-related toxicity in older patients with cancer, which has also been validated in an independent cohort study of 250 older adults ( $\geq 65$  years) with a solid tumor.<sup>59,60</sup> The following factors were predictive of grade 3 to 5 toxicity: age greater than or equal to 72 years; type of cancer (gastrointestinal [GI] or genitourinary); standard-dose chemotherapy; polychemotherapy; hemoglobin level (male:  $< 11$  g/dL; female:  $< 10$  g/dL); creatinine clearance less than 34 mL/min; hearing impairment described as fair or worse; one or more falls in the last 6 months; limited in walking one block; the need for assistance with taking medications; and decreased social activities due to physical or emotional health. Extermann et al have developed the chemotherapy risk assessment scale for high-age patients (CRASH) score, which could be useful in predicting significant differences in the risk of severe toxicity in older patients with cancer starting a new chemotherapy.<sup>61</sup> In this model, diastolic blood pressure, IADLs, lactate dehydrogenase, and the type of treatment were the best predictors of hematologic toxicity. Performance status, cognitive function, nutritional status, and the type of therapy were the best predictors of non-hematologic toxicity. These tools can aid the oncologist in selecting

and discussing the recommended therapy with an older adult. Such information will allow for shared decision-making weighing the risks and benefits of the proposed treatment approach. A study showed the benefits of performing CGA prior to chemotherapy and delivering CGA guided care along side anti-cancer therapy in reducing toxic effects in older adults with cancer. In this randomized controlled trial (RCT), 613 patients 65 years of age or older were randomized to either the specific geriatric assessment-driven intervention (GAIN) arm or to the standard of care (SOC) arm. Incidence of grade 3 or higher chemotherapy-related toxic effects in the GAIN arm (50.5%; 95% CI, 45.6%–55.4%) were 10.1% lower than the SOC arm (60.6%; 95% CI, 53.9%–67.3%).<sup>229</sup> Another study, the Geriatric Assessment for Patients 70 years and older (GAP70+) trial, also reported a significant reduction in the proportion of patients with grade 3 to 5 toxic effects who were assigned to geriatric assessment intervention before receiving chemotherapy (51% vs. 71% with usual care; relative risk [RR], 0.74; 95% CI, 0.64–0.86;  $P = .0001$ ).<sup>230</sup>

### Targeted Therapy

The emergence of targeted therapies (monoclonal antibodies and small molecules targeted against specific molecular pathways required for the development of a particular malignancy) has significantly improved outcomes in a variety of malignancies. The use of targeted therapies in older patients appears to be promising in view of their better efficacy and toxicity than conventional chemotherapeutic agents.<sup>231,232</sup> However, these drugs are also associated with some unique and severe side effects.<sup>233</sup> For example, cardiovascular complications such as left ventricular dysfunction (LVD) are associated with HER2 inhibitors (trastuzumab) and hypertension and arterial thromboembolic events (ATEs) are associated with vascular endothelial growth factor receptor (VEGFR) inhibitors (ie, bevacizumab),<sup>234-236</sup> whereas dermatologic toxicities (acneiform rash and hand-foot skin reaction) are the major adverse effects of EGFR inhibitors (ie, erlotinib, sunitinib, sorafenib, cetuximab).<sup>237</sup>



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There are limited but growing data available on the safety and efficacy of targeted therapies in older patients with cancer. Prospective clinical trials that include a sufficiently large number of older patients are needed to accurately determine the efficacy and tolerability of targeted therapies in this cohort of patients. In patients who are not able to tolerate cytotoxic chemotherapy, the risk-benefit ratio should be considered prior to initiation of targeted therapy and the use of targeted therapies should be individualized.

### **Immunotherapy (including chimeric antigen receptor [CAR] T-cell therapy)**

Older adults are underrepresented in clinical trials studying immunotherapy including CAR T-cell therapy across multiple cancers. Participation of this population is limited due to exclusion criteria in studies related to age, comorbidities, and impaired functional status.<sup>238</sup> In general, information derived from subgroup analyses and retrospective studies report a similar clinical benefit in older and younger patients in case of immune checkpoint inhibitor (ICI) therapy (ie, PD-1/PD-L1),<sup>239,240</sup> with some concerns for increase in toxicity rates. In the Keynote-024 study of pembrolizumab for NSCLC patients with more than half of the population being older than 65 years, a more favorable HR of 0.45 (0.29–0.70; 95% CI) for disease progression or death was observed for older patients compared to younger ones.<sup>241,242</sup> Subgroup analysis of the Keynote-045 phase 3 study evaluating benefits of pembrolizumab over chemotherapy in older patients aged 65 years and older with advanced urothelial carcinoma, who had progressed after chemotherapy, showed improved OS and fewer adverse events in the pembrolizumab group.<sup>243</sup> Similarly, in a meta-analysis of 34 RCTs with 21,213 patients with advanced cancers (eg, NSCLC, melanoma), which included 69.4% of patients younger than 65 years and 40.6% of patients aged 65 years and older, similar statistically significant advantage in OS of immunotherapy over control

therapy (non-ICI therapy) was observed in both age groups.<sup>240</sup> A meta-analysis evaluated 15 phase 3 studies that included patients aged 75 years or more with NSCLC, renal cell carcinoma (RCC), melanoma, head and neck squamous cell carcinoma (SCC), or gastric cancer comparing ICI therapies (mono- or combination therapy) versus standard therapy as first-line and second-line treatment. The HR for the first-line setting was 0.78 (95% CI, 0.61–0.99) versus 1.02 (95% CI, 0.77–1.36) for second-line treatment, which indicated survival benefits of ICI therapy in the first-line setting but not in second-line treatment.<sup>244</sup>

Safety data of CAR T-cell therapies in the older patient population are sparse that limit the generalization of the effects of CAR T-cell therapy in the older population. The pivotal ZUMA-1 phase 1/2 study evaluating safety of a CAR T-cell therapy for B-cell lymphoma showed no significant differences in the extent of benefits between younger and older patients, although the older patients only represented a small number.<sup>245</sup> In a large-scale post-marketing analysis of 804 cases receiving CAR T-cell therapy,<sup>246</sup> some of the adverse events noted in older patients receiving CAR T-cell therapy versus the younger population were encephalopathy syndrome (8% vs. 4%,  $P = .03$ ), decreased hemoglobin and hematocrit (13% vs. 7% and 12% vs. 6%, respectively;  $P < .01$  for both), decreased blood fibrinogen (2% vs. 0.2%,  $P = .04$ ), increased blood creatinine (2% vs. 0.2%,  $P = .04$ ), rash (2% vs. 0%,  $P < .01$ ), and sepsis (3% vs. 1%,  $P = .02$ ). Younger patients reported more hospitalizations and adverse events such as pyrexia, tachycardia, and thrombocytopenia.<sup>246</sup>

As these treatments carry risks for immune-related adverse events, we must consider the nuances of managing these types of toxicities in older adults. High-dose steroids for the management of immune-related toxicities must be used with caution in older patients as they may worsen other comorbidities or cognitive function. The NCCN Panel recommends that when steroids are being used for supportive care, careful



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consideration must be given to the dose and duration of therapy, and for management of immunotherapy-related adverse events, lowest possible effective dose should be used.

### Management of Side Effects in Older Adults Undergoing Cancer-Specific Treatment

In older patients undergoing chemotherapy, the most common complications include myelosuppression resulting in neutropenia, anemia, or thrombocytopenia; mucositis; renal toxicity; cardiac toxicity; and neurotoxicity. Older patients appear to be at special risk for severe and prolonged myelosuppression and mucositis, increased risk for cardiomyopathy, and increased risk for peripheral neuropathy. In addition, they are also at risk for infection (with or without neutropenia), dehydration, electrolyte disorders, and malnutrition either as a side effect of the chemotherapy or directly from the tumor. Chemotherapy can also affect cognition, function, balance, vision, hearing, continence, and mood.<sup>247</sup> The combination of these complications enhances the risk of delirium and functional dependence. It is essential to detect and correct these complications (that may interfere with treatment) in order to achieve maximum benefit from chemotherapy. Prevention and/or amelioration of some of the common chemotherapy-related complications are discussed below.

#### *Cardiovascular Toxicity*

Anthracyclines are associated with increased cardiac toxicity resulting in LVD and CHF.<sup>248,249</sup> Other antineoplastic drugs associated with significant cardiovascular complications include alkylating agents, antimetabolites, microtubule-stabilizing agents, and targeted therapies such as trastuzumab and immunotherapies. These drugs may have an additional effect on anthracycline-induced cardiovascular toxicity. Risk factors for anthracycline-induced cardiovascular toxicity include an existing or history of heart failure or cardiac dysfunction, hypertension, diabetes and CAD,

older age (independent of comorbidities and performance status), prior treatment with anthracyclines, higher cumulative doses, and short infusion duration.<sup>249,250</sup>

Cardiac toxicity in older patients receiving trastuzumab remains a concern.<sup>251-254</sup> Increased incidence of cardiotoxicity are seen among older patients with breast cancer with a history of cardiac disease and/or diabetes treated with trastuzumab.<sup>254</sup> In a large, population-based, retrospective study of older patients with stage I–III breast cancer ( $\geq 66$  years; 9535 patients; 2203 patients received trastuzumab), the use of trastuzumab resulted in a CHF rate of 30%, which is substantially higher than that reported in clinical trials. Among patients treated with trastuzumab, older age ( $\geq 80$  years), hypertension, CAD, cardiac comorbidities, and weekly administration of trastuzumab were associated with increased risk of CHF.<sup>255</sup> In general, taxane-anti-HER2 combinations without anthracyclines and with close cardiac monitoring are recommended for older patients. Although investigated in the general population of lower-risk adjuvant breast cancer patients, the combination of paclitaxel and trastuzumab is associated with excellent outcomes and tolerability.<sup>256</sup>

Emerging data from clinical studies suggest that trastuzumab, when used in combination with non-anthracycline–based chemotherapy, has similar efficacy with lower rates of cardiac events in patients with early-stage as well as metastatic HER2-positive breast cancer.<sup>257-259</sup> The subgroup analysis of the randomized trial that evaluated trastuzumab in combination with docetaxel and pertuzumab in patients with HER2-positive metastatic breast cancer (808 patients; 127 patients were  $\geq 65$  years) did not show any increase in the risk of cardiac dysfunction associated with trastuzumab, and there was also no evidence of late or cumulative cardiac toxicity.<sup>259</sup> In addition, the results also showed no significant correlation between age and the development of left ventricular systolic dysfunction in



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older patients. Additional data are needed regarding the tolerability of these regimens in older patients.

Cardiac toxicity from immunotherapy is rare but can include arrhythmias, myocarditis, and heart failure, which could lead to severe consequences including death. Prevalence is much higher in patients on combination immunotherapy.<sup>260</sup>

### *Renal Toxicity*

The GFR decreases with age, which in turn delays elimination of many drugs. Delayed renal excretion may enhance the toxicity of medications whose parent compounds are excreted by the kidneys (ie, carboplatin, oxaliplatin, methotrexate, bleomycin) and drugs that are converted to active (ie, idarubicin, daunorubicin) or toxic metabolites (ie, high-dose cytarabine).<sup>5</sup> Dose adjustment to the measured GFR should be considered for these drugs to decrease systemic toxicity.

Renal insufficiency is common in older patients with cancer, particularly in patients receiving nephrotoxic drugs, patients with genitourinary cancers, or patients with multiple myeloma. In patients with preexisting renal problems who are at a greater risk of renal impairment, the use of nephrotoxic drugs should be limited or avoided. 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.

### *Neurotoxicity*

Neurotoxicity is also a dose-limiting toxicity associated with chemotherapy.<sup>261</sup> Vinca alkaloids, platinum-based therapies, and taxanes induce peripheral neurotoxicity. Methotrexate, cytarabine, and ifosfamide are associated with central neurotoxic side effect. Purine analogs (eg, fludarabine, cladribine, pentostatin) are associated with life-threatening neurotoxicity at significantly higher doses than the recommended clinical

dose.<sup>262</sup> High-dose cytarabine can cause an acute cerebellar syndrome. Patient's age (>60 years), drug dose and schedule, and renal and hepatic dysfunction are the most important risk factors for cytarabine-induced cerebellar toxicity.<sup>263,264</sup>

Management of neurotoxicity mainly consists of dose reductions or lower dose intensities. Older patients are particularly susceptible to the toxicity of cytarabine-based regimens due to decreased renal excretion of the toxic metabolite ara-uridine, and increased vulnerability of the cerebellum. Particular attention should be paid to the use of cytarabine in high doses, especially in patients with renal insufficiency. Dose reductions are necessary in patients with reduced GFR. The Guidelines recommend monitoring for cerebellum function, hearing loss, and peripheral neuropathy. The risk of falls due to peripheral neuropathy is of particular concern in older patients.<sup>185</sup>

### *Myelosuppression*

Available data from various studies have shown that the risk of myelosuppression increases substantially by age 65 years.<sup>265-269</sup> The risk of myelosuppression is decreased by 50% when using growth factors.<sup>270-272</sup> The use of growth factors in these circumstances does not appear to be associated with increased cost and may even be cost saving if it prevents lengthy hospitalizations from neutropenic infections in older persons.

### *Neutropenia*

Neutropenia is the major dose-limiting toxicity associated with chemotherapy, especially in older patients. Among older patients with aggressive non-Hodgkin lymphoma treated with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy, the incidences of fever and neutropenia were significantly higher for patients aged greater than or equal to 70 years (42% vs. 8% for



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patients aged 61–69 years;  $P < .0001$ ).<sup>273</sup> In patients 60 years or older receiving induction or consolidation chemotherapy for AML, the prophylactic use of hematopoietic growth factors results in faster recovery of neutrophil and shorter hospitalization, but it does not impact OS.<sup>274,275</sup>

Meta-analysis of controlled clinical trials on the prophylactic use of recombinant granulocyte colony-stimulating factors (G-CSF) has confirmed their effectiveness in reducing the risk of febrile neutropenia.<sup>276</sup> The use of growth factors appears to be the best established strategy to improve treatment in older patients.<sup>277</sup> The EORTC has issued recommendations for the prophylactic use of G-CSF in older patients with cancer.<sup>278</sup> The NCCN Guidelines for Myelodysplastic Syndrome available at [www.NCCN.org](http://www.NCCN.org) address the use of G-CSFs in patients with solid tumors and non-myeloid malignancies.

### Anemia

Anemia has been shown to be a risk factor for chemotherapy-related toxicity and is one of the factors responsible for the reduction in volume of distribution, which may result in increased peak concentration and increased toxicity of drugs.<sup>279</sup> Anemia is also associated with cardiovascular disease, CHF, CAD, and dementia.<sup>280–283</sup> In older patients of aged 65 years or more with cancer, anemia is significantly associated with multidimensional loss of function (eg, mobility limitations, impaired cognition) and higher rates of functional disability.<sup>284,285</sup>

In patients with severe anemia, blood transfusions may be necessary to prevent serious clinical consequences. Although erythropoiesis-stimulating agents (ESAs) have been demonstrated to decrease the need for transfusion in patients receiving chemotherapy,<sup>286</sup> randomized studies have reported decreased survival and poorer tumor control among patients with cancer receiving erythropoietic drugs for correction of anemia

and target hemoglobin levels 12 g/dL.<sup>287</sup> The use of ESAs in patients with cancer is also associated with increased risks of venous thromboembolism and mortality.<sup>288,289</sup> In July 2008, based on the results of these trials, the FDA strengthened its warnings to alert physicians of increased risk of tumor progression and shortened survival in patients with advanced breast, cervical and head and neck cancers, lymphoid neoplasms, and NSCLC. Physicians were advised to use the lowest dose necessary to avoid transfusion. In addition, the use of ESAs is restricted to the treatment of anemia specifically related to myelosuppressive chemotherapy without curative intent. ESAs should be discontinued once the course of chemotherapy has been completed and the anemia has resolved. Evaluation of deficiency in iron, B12 and folic acid should be conducted in the setting of anemia with initiation of the appropriate replacement therapy is recommended. The panel recommends that anemia in older patients with cancer should be managed as outlined in the NCCN Guidelines for Hematopoietic Growth Factors available at: [www.NCCN.org](http://www.NCCN.org).

### Thrombocytopenia

Chemotherapy-induced thrombocytopenia (CIT) is a common hematologic toxicity associated with cytotoxic and myeloablative chemotherapy. Dose reductions and/or interruptions of chemotherapy regimens are necessary in patients with severe thrombocytopenia. While chemotherapy-induced anemia and neutropenia can be managed with hematopoietic growth factors, safe and effective treatment of CIT is still a significant problem. Recombinant interleukin-11 is the only currently approved treatment of CIT in patients with non-myeloid malignancies.<sup>290</sup> However, it is toxic and of minimal clinical benefit. A phase II clinical trial demonstrated significant efficacy of thrombopoietin-like agents such as romiplostim and eltrombopag for the treatment of CIT; however, the settings for which these agents will provide clinical benefit are important and not yet fully defined in older patients.<sup>291,292</sup> Current recommendations



include the management of CIT in older patients similar to the younger patient population.

### *Nausea and Vomiting*

Chemotherapy-induced nausea and vomiting (CINV) is a debilitating side effect that can significantly affect a patient's QOL and compliance with treatment. In addition, older adults maybe at higher risk for dehydration and other complications as a result of significant nausea and vomiting. Serotonin (5-HT3)-receptor antagonists, neurokinin-1-receptor antagonists, and corticosteroids are the most effective antiemetic drugs used for the management of CINV.<sup>293</sup> Older patients may have an increased risk of toxicity from antiemetic drugs due to age-related physiologic changes in drug absorption, distribution and excretion, drug interactions, and polypharmacy used to treat comorbidities.<sup>294,295</sup> Therefore, the selection of appropriate antiemetic therapy in older patients should be based on individual patient characteristics, prior history of CINV, the emetogenic potential of the specific chemotherapeutic agent, and most importantly the side effect profile of the antiemetic agent. For example, QTc prolongation has been reported as a class effect of 5-HT3-receptor antagonists, especially dolasetron, tropisetron, and palonosetron, and these should be used with caution in older patients with cardiovascular complications.<sup>294</sup> CINV should be managed as described in the NCCN Guidelines for Antiemesis and the NCCN Guidelines for Palliative Care available at [www.NCCN.org](http://www.NCCN.org).

### *Diarrhea*

Diarrhea is a well-recognized side effect associated with a number of chemotherapeutic agents, particularly fluorouracil and irinotecan. Loss of fluids and electrolytes associated with persistent and severe diarrhea can lead to dehydration, renal insufficiency, and electrolyte imbalance.<sup>296</sup> Furthermore, chemotherapy-induced diarrhea can lead to dose reductions, delay in therapy, or discontinuation of chemotherapy, which ultimately

affect clinical outcomes.<sup>297</sup> Based on the results from various clinical trials, the ASCO guidelines for the comprehensive evaluation and management of cancer treatment-induced diarrhea recommend loperamide as the standard therapy for mild-to-moderate diarrhea.<sup>296</sup> Octreotide (subcutaneous or intravenous if the patient is severely dehydrated) may be beneficial for patients with severe diarrhea or diarrhea that is refractory to loperamide therapy. Diphenoxylate/Atropine (oral opiate) therapy is also occasionally prescribed for cancer treatment-induced diarrhea with mild symptoms (although loperamide is preferred) and is used with extreme caution in patients with renal and/or liver failure.<sup>298</sup>

The NCCN Guidelines recommend early aggressive rehydration and management with octreotide (if oral treatments are ineffective) for older patients with chemotherapy-induced diarrhea.

### *Mucositis*

Oral and GI mucositis are significant complications of radiotherapy and chemotherapy. The risk of mucositis increases with age, and its presence in older adults can lead to decreased oral intake, leading to dehydration and additional complications. In a phase III randomized study of 212 patients with hematologic cancers undergoing high-dose chemotherapy and total body irradiation followed by autologous HCT, palifermin (human keratinocyte growth factor) was associated with a significant reduction of oral mucositis compared to placebo (20% vs. 62%).<sup>299</sup> Palifermin is approved for the treatment of oral mucositis in patients with hematologic malignancies receiving myeloablative therapy requiring hematopoietic stem cell support. A few studies have reported that palifermin is also well tolerated and effective in the prevention of oral mucositis in patients with metastatic CRC treated with fluorouracil-based chemotherapy and in patients with head and neck cancer treated with postoperative or definitive chemoradiation therapy.<sup>300-302</sup> The 2014 Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology



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have detailed recommendations for the management of mucositis secondary to cancer therapy.<sup>303</sup> Once mucositis has occurred, patients should be kept well hydrated with intravenous fluids. Early hospitalization may be necessary for patients with mucositis who also develop dysphagia or diarrhea.

### *Insomnia*

Insomnia is characterized by difficulty falling or staying asleep, waking up too early, or experiencing poor-quality nonrestorative sleep associated with daytime impairment (fatigue, poor concentration, daytime sleepiness, or concerns about sleep).<sup>304</sup> The incidence of insomnia in patients with cancer has been reported to be three times higher than that reported in the general population and ranges from 25% to 69%, depending on the type of cancer.<sup>305,306</sup> In a longitudinal study that assessed the prevalence and natural course of insomnia in patients with cancer during an 18-month period, Savard et al reported higher rates of insomnia in patients with breast (42%–69%) and gynecologic (33%–68%) cancer and lower rates among those with prostate cancer (25%–39%).<sup>306</sup>

Insomnia is more prevalent in older adults, and older patients with cancer should be screened for sleep disturbances prior to the initiation of treatment and at regular intervals during the course of treatment. The AGS has provided recommendations for the diagnosis, evaluation, and management of insomnia in older adults.<sup>304</sup> The published Pan-Canadian practice guidelines also provide recommendations for the prevention, screening, assessment, and treatment of sleep disturbances in older patients with cancer.<sup>307</sup>

Cognitive behavioral therapy (CBT) and lifestyle modifications are the preferred first-line treatment options for the management of insomnia in older patients.<sup>304,307</sup> The effectiveness of CBT with multicomponent interventions (stimulus control, sleep restriction, cognitive therapy, sleep hygiene, and fatigue management) for the management of insomnia in

patients with cancer has been demonstrated in randomized clinical trials.<sup>308–311</sup> Adherence to CBT has been shown to yield greater sleep improvements among patients following primary treatment for breast cancer.<sup>312</sup>

Pharmacologic therapy may be necessary for some patients until CBT takes effect.<sup>304,307</sup> Benzodiazepines, non-benzodiazepines, and melatonin-receptor agonists are the FDA-approved classes of drugs for the treatment of insomnia.<sup>313,314</sup> However, due to some of the severe adverse effects associated with benzodiazepines and non-benzodiazepines (eg, impaired postural stability, fractures, cognitive impairment),<sup>313</sup> these drugs are not recommended as first-line therapy for the treatment of insomnia in older adults.<sup>304,307</sup> Patients should be cautioned that most over-the-counter sleep medications contain antihistamines that carry risk of toxicities in older adults and thus should be avoided if possible. If pharmacologic therapy is to be utilized, it is recommended only for short-term use, with the lowest dose that is safe and effective to address the particular type of sleep disturbance in an individual patient. The risks and benefits of the therapy should be discussed. The panel notes that if zolpidem is considered, the FDA has advised that the recommended dose of zolpidem for patients assigned female at birth should be lowered.<sup>315</sup>

### **Adherence to Therapy**

Adherence to the prescribed regimen, especially oral therapy, is essential to derive maximal clinical benefit. While older age per se is not a consistent risk factor for non-adherence, older adults are at an increased risk for non-adherence for a variety of reasons, including cognitive impairment, increased number of comorbid conditions, polypharmacy, higher risk of side effects adversely affecting comorbidities, increased likelihood of drug interactions, limited insurance coverage, social isolation, and inadequate social support.<sup>316</sup> Treatment-related adverse events,



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complexity of regimens, and poor understanding of the need for treatment are some of the other common barriers to adherence.

Discontinuation and nonadherence to adjuvant hormonal and chemotherapies are well documented in patients with early-stage breast cancer. In studies that have evaluated adherence to adjuvant hormonal therapy (ie., tamoxifen) among older patients ( $\geq 55$  years) diagnosed with early-stage breast cancer, the reported rates of nonadherence or discontinuation range from 15% to 49%.<sup>317-321</sup> In the randomized study (CALGB 49907) that evaluated adjuvant chemotherapy with oral capecitabine versus standard chemotherapy in 161 patients ( $\geq 65$  years) with early-stage breast cancer, 25% of the patients took fewer than 80% of the planned doses.<sup>322</sup> Adherence was not related to age, tumor stage, or hormone receptor status. However, in other studies, poor adherence to adjuvant chemotherapy was more frequent in older patients ( $\geq 65-75$  years).<sup>323,324</sup> In the ADAGIO study, non-adherence was associated with poorer response to imatinib in patients with chronic myeloid leukemia (CML); non-adherence rates were significantly higher for patients with suboptimal response compared to those with optimal response to imatinib (23% and 7%, respectively).<sup>325</sup> Marin and colleagues also identified adherence as the only independent predictor for achieving complete molecular response on standard-dose imatinib in patients with CML.<sup>326</sup> Adherence to chemotherapy also significantly reduced the risk of cancer-related mortality in patients with stage III colon cancer with [RR], 0.79 (95% CI = 0.69 to 0.89), with greater non-adherence observed in those with cancer recurrence (for adjuvant therapy completion, [RR], 0.22, 95% CI = 0.14-0.31). The likelihood of completing the cancer treatment decreased with age, with those older than 75 years were less likely to complete adjuvant chemotherapy.<sup>327</sup> In patients of age 66 years and older with local or regional head and neck cancer, adherence was more common in the patients receiving surgical procedures prior to radiotherapy

as compared to the patients who receive radiotherapy alone or in combination with chemotherapy.<sup>328</sup>

Few studies have determined the actual adherence to oral therapies in patients with cancer, but clinical trials in a variety of cancer types attribute reduced adherence in older patients to toxicity. A task force report from SIOG that reviewed the impact of age-related factors on adherence to oral therapy in older adults recommends careful patient selection (using CGA, mentioned above, or other geriatric screening tools) and close monitoring of adherence to oral therapy.<sup>329</sup> The task force report summarizes all potential determinants of adherence in older adults as attributed to factors that may be patient-related, age-specific, socioeconomic, disease-related, therapy (toxicity)-related, or health care team-associated. Since non-adherence is a complex issue associated with increased mortality and health care costs, the task force has also compiled a corresponding set of health care-led and patient-driven intervention strategies to promote adherence and overcome the barriers to adherence.

In older patients with cancer, assessment of risk factors for non-adherence is recommended when considering a treatment regimen that will include an oral agent. Close monitoring of patient adherence; reduction of regimen complexity (if possible); interventions designed to educate older patients about the risks and benefits of oral therapy and the importance of adherence to therapy; adequate and appropriate management of side effects; and scheduling of follow-up visits at regular intervals to review side effects are some strategies that may be helpful to minimize non-adherence to therapy. In addition, prioritizing the clinical pharmacists' involvement in adherence management especially for patients receiving oral anti-cancer therapies is recommended.<sup>330</sup> Muluneh et al executed an integrated, closed-loop, pharmacy-led oral chemotherapy management program within their institution to provide specialty pharmacy services to their patients to facilitate their copays, prior authorizations, clinical



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education, refill follow-up via phone calls, dispensation, home delivery, etc. Their program also credentialed the clinical pharmacists in oncology to educate and counsel patients starting oral chemotherapy either via phone or in clinic, as well as assess the patient's adherence to medication.

Patient's understanding and assessment of adherence was evaluated via pre-tests, post-tests, and follow-up questions. The results showed an increase in comprehension of oral chemotherapy treatment from 43% to 95%. Adherence rates for the GI/breast and malignant hematologic patient populations were 85% and 93.9%, respectively.<sup>330</sup>

### Approach to Cancer Screening and Surveillance Testing

Cancer screening refers to screening for new primary cancers that are different than the cancer survivor's prior cancer. The older adults with cancer often have multiple chronic conditions that could decrease their life expectancy.<sup>331</sup> Although screening older adults could be beneficial in detecting cancers at early stages to allow for early intervention strategies, one major downside is overdiagnosis and treatment of cancers that might not have caused any symptoms during the patient's lifetime.<sup>332</sup> Harms of screening relevant to older adults include fatigue from tests, discomfort, side effects, harms of procedure after-care, and distracting/time consuming. Moreover, the direct benefits of cancer screening are less evident specifically for this population since the RCTs of screening rarely include older age groups.<sup>331</sup> There is some evidence to support routine screening for the following cancers (although evidence in older individuals is limited): breast, colorectal, and lung cancer. In a retrospective cohort study with 5186 patients with breast cancer aged 65 and older, mammogram screening of breast cancer was associated with reduction in risk of death for all patients with mild to moderate comorbidities; however, those with severe or multiple comorbidities showed no improvement in OS.<sup>333</sup> The American Cancer Society recommends mammography in older patients who have a life expectancy of 10 years or more, as it is unlikely to benefit those with less than a 10-year life expectancy. Screening decisions

among patients aged 75 years and older should be made according to overall health and patient preferences.<sup>334</sup> Several trials have shown benefits of CRC screening such as sigmoidoscopy, fecal occult blood testing, and CT colonography and/or colonoscopy in older patients in reducing CRC-specific mortality rates.<sup>335</sup> However, colonoscopy was associated with serious adverse events in asymptomatic persons including perforations and bleeding and is not recommended for persons with less than a 10-year life expectancy or those aged 85 years and older. There is limited or no evidence to support screening for cervical cancer or prostate cancer in older people. False-positive of abnormal pap smear is common in older patients due to difficulty obtaining an adequate sample. Cervical cancer growth is slow and can take 10 to 30 years, and there is a possibility of spontaneous regression of low-grade cervical lesions in older adults.<sup>332</sup> In addition, pap smears are associated with high anxiety and psychological distress. Data are lacking to demonstrate any benefit in prostate cancer screening for patients older than 75 years. For patients aged 55 to 74 years, the U.S. PLCO trial of over 75,000 patients found no benefits,<sup>336</sup> although younger patients with no comorbidities showed reduction in prostate cancer-specific mortality rates with screening.<sup>337</sup>

Hence, routine cancer screening should be performed on older adult patients after careful consideration of their overall life expectancy. If the patient's life expectancy is 10 years or less, the patient is unlikely to benefit from routine cancer screening and more likely to experience immediate harms and distress. Thus, cancer screening should be stopped for such patients. If the patient's life expectancy is greater or equal to 10 years, the patient's goals and values must be consistent with wanting treatment if the cancer is detected to warrant continuation of routine screening.<sup>332</sup>

"Surveillance screening" refers to routine screening (in the absence of symptoms or abnormal physical examination findings) for recurrence or



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new primary cancers of the same type as the cancer survivor's prior cancer(s) beyond routine history and physical examination. (Note that diagnostic evaluation is recommended for any patient with symptoms or signs suspicious for cancer recurrence on history or physical examination.) If the patient's life expectancy is 5 years or less, they are unlikely to benefit from routine surveillance testing. The NCCN Panel recommends stopping routine surveillance testing for these patients in the absence of symptoms or findings on physical examination. If the patient's life expectancy is greater than 5 years, the patient's goals and values must be consistent with wanting treatment should cancer recurrence be detected, the health status should be appropriate, and individualized, shared decision-making should be engaged when determining the need for routine surveillance testing.

The benefits of cancer screening and routine surveillance testing are likely to exceed the harms of screening if the patient's risk of cancer is higher than average (eg, genetic cancer syndrome, prior exposures such as radiation or chemotherapy) and if life expectancy is sufficient (>5 years). The harm of screening and surveillance testing will outweigh the benefit in the setting of significant comorbidities, which can limit the ability to conduct the test (eg, colonoscopy in the setting of significant cardiac or lung disease) or impact ability to treat cancer if detected. For example, patients with favorable-subtype breast cancers treated with endocrine therapy carry a lower risk of recurrence/new primaries compared to similar-aged patients with no history of breast cancer, and thus are not likely to benefit from routine surveillance testing.<sup>338</sup>

## Summary

There are unique issues to consider when caring for an older adult with cancer. The physiologic changes associated with aging may impact an older adult's ability to tolerate cancer therapy and should be considered

in the treatment decision-making process. Nevertheless, advanced age alone should not be the only criterion to preclude a patient from receiving effective cancer treatment that could improve QOL or lead to a survival benefit. Treatment should be individualized based on the nature of the disease, the physiologic status of the patient, and the patient's preferences.

Appropriate use of geriatric screening tools and/or CGA enables physicians to develop a coordinated plan for cancer treatment as well as guide interventions tailored to the individual patient based on his/her functional status and physiologic age rather than chronologic age. The goal of the NCCN Guidelines for Older Adult Oncology is to assist clinicians in providing evidence-based oncology care that enhances treatment decision-making and improves QOL in older adults with cancer. The updated guidelines include a roadmap that could assist providers in tailoring a geriatric assessment that could be routinely used in their clinical practice as they provide care to this vulnerable patient population.



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