



Comprehensive Geriatric Assessment and Clinical Outcome in Elderly Patients with Acute Leukemia

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Epidemiology and Current Challenges:

- AML is a common hematologic malignancy in adult patients.
- Incidence of AML increases with advancing age.
- A recent study showed a total of 7007 cases of AML were diagnosed in California between 1999 and 2014, with patients aged over 65 accounting for 36.4% of the cases.
- The cut-off age for elderly AML is **60 years**.
- Elderly patients with AML have a **poorer prognosis** than younger patients.

Epidemiology and Current Challenges:

- Patients aged 60-65 years have a **5-year OS of 25%**, whereas the 5-year OS for patients aged less than 50 is 50%.
- Factors associated with adverse outcomes in elderly AML
 - Poor performance status (PS)
 - Multiple comorbidities
 - High-risk cytogenetic abnormalities
 - High-risk molecular mutations
 - High mortality rate after receiving induction chemotherapy.



Epidemiology and Current Challenges:

Figure 1 Overall Survival Curves of Younger and Older Age Groups ($P < .001$)

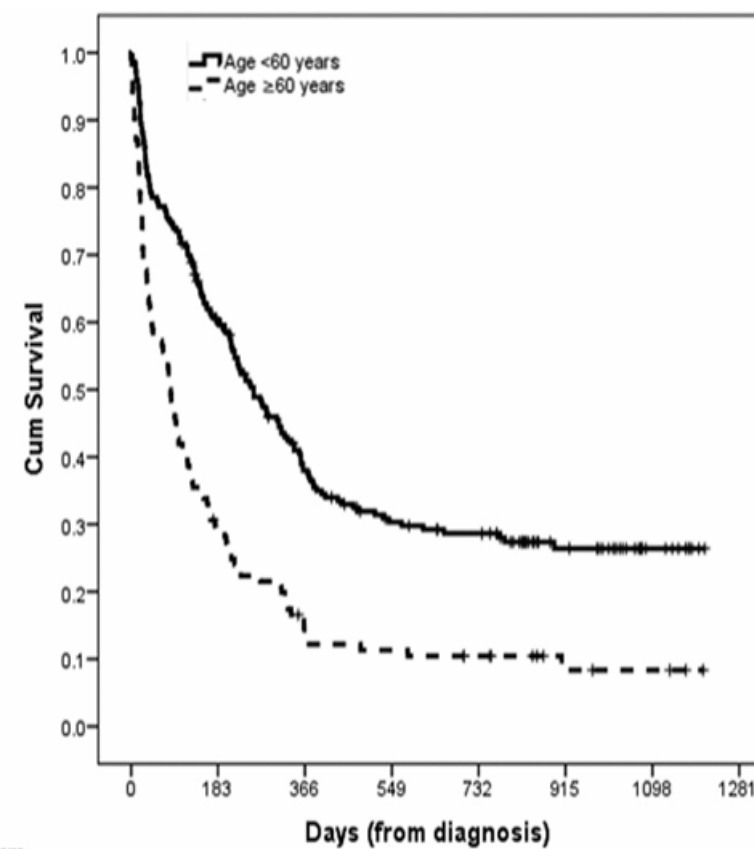
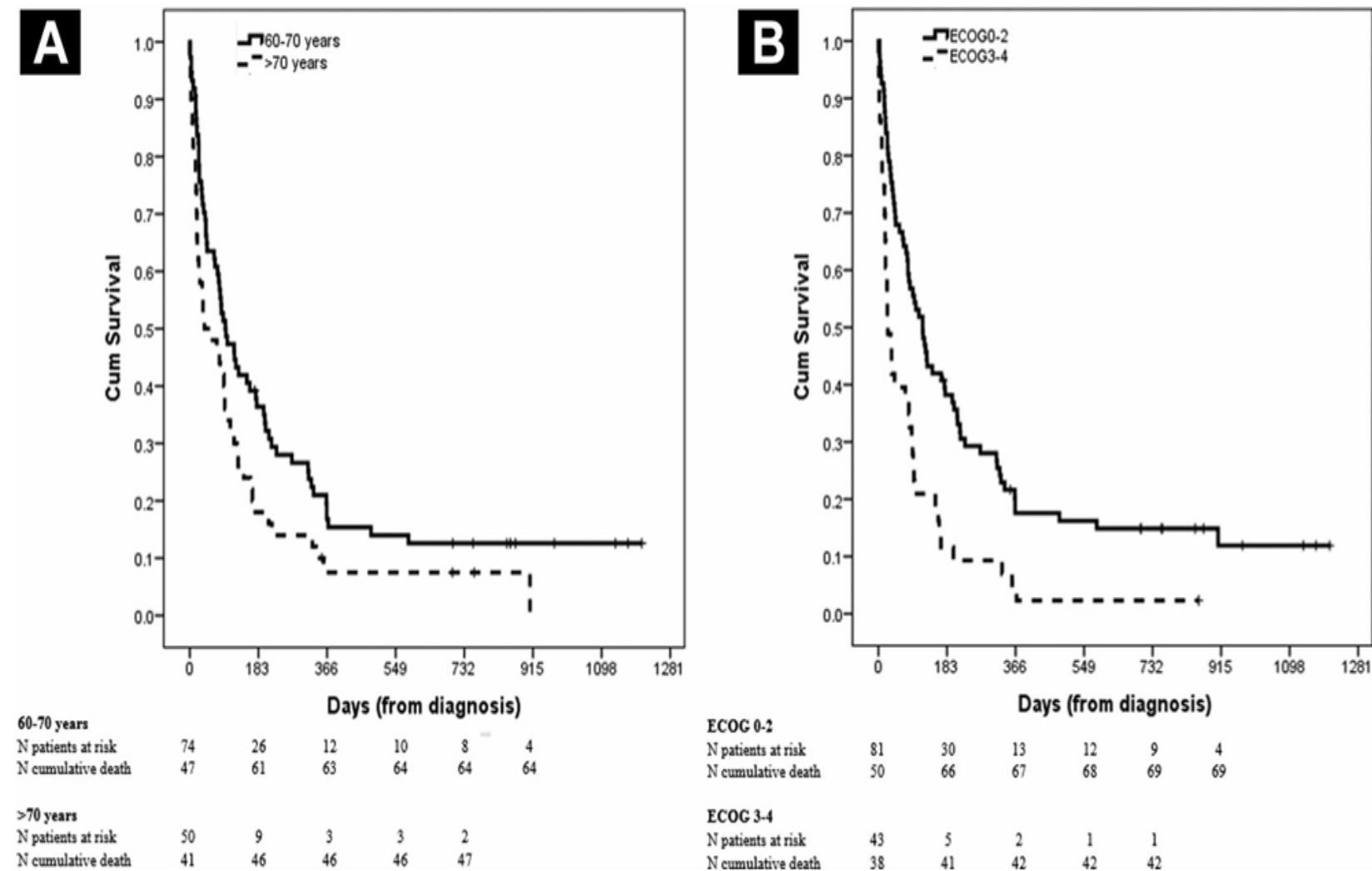
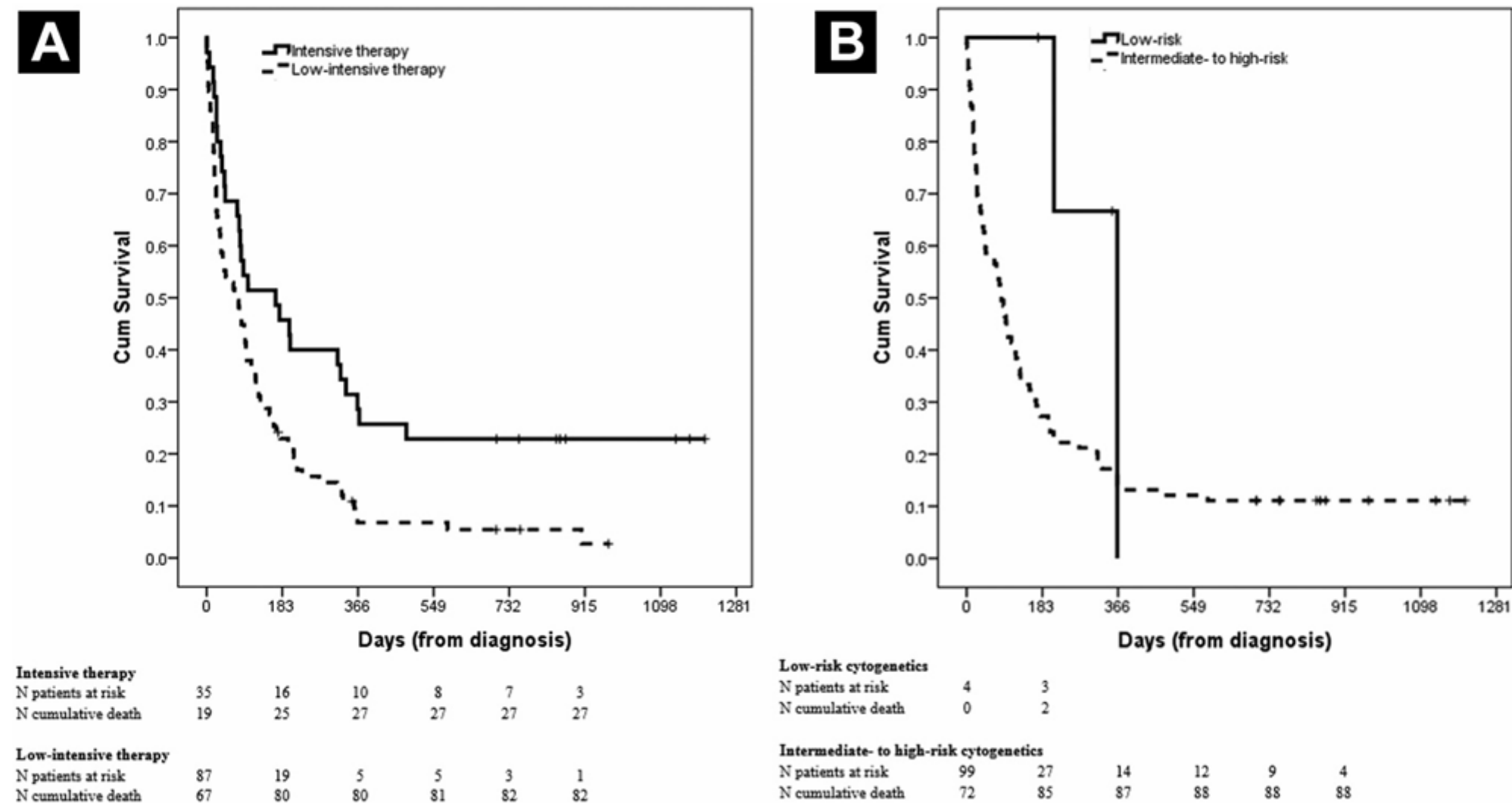


Figure 2 Overall Survival Curves according to Age Groups ($P = .025$) (A) and ECOG PS ($P < .001$) (B)

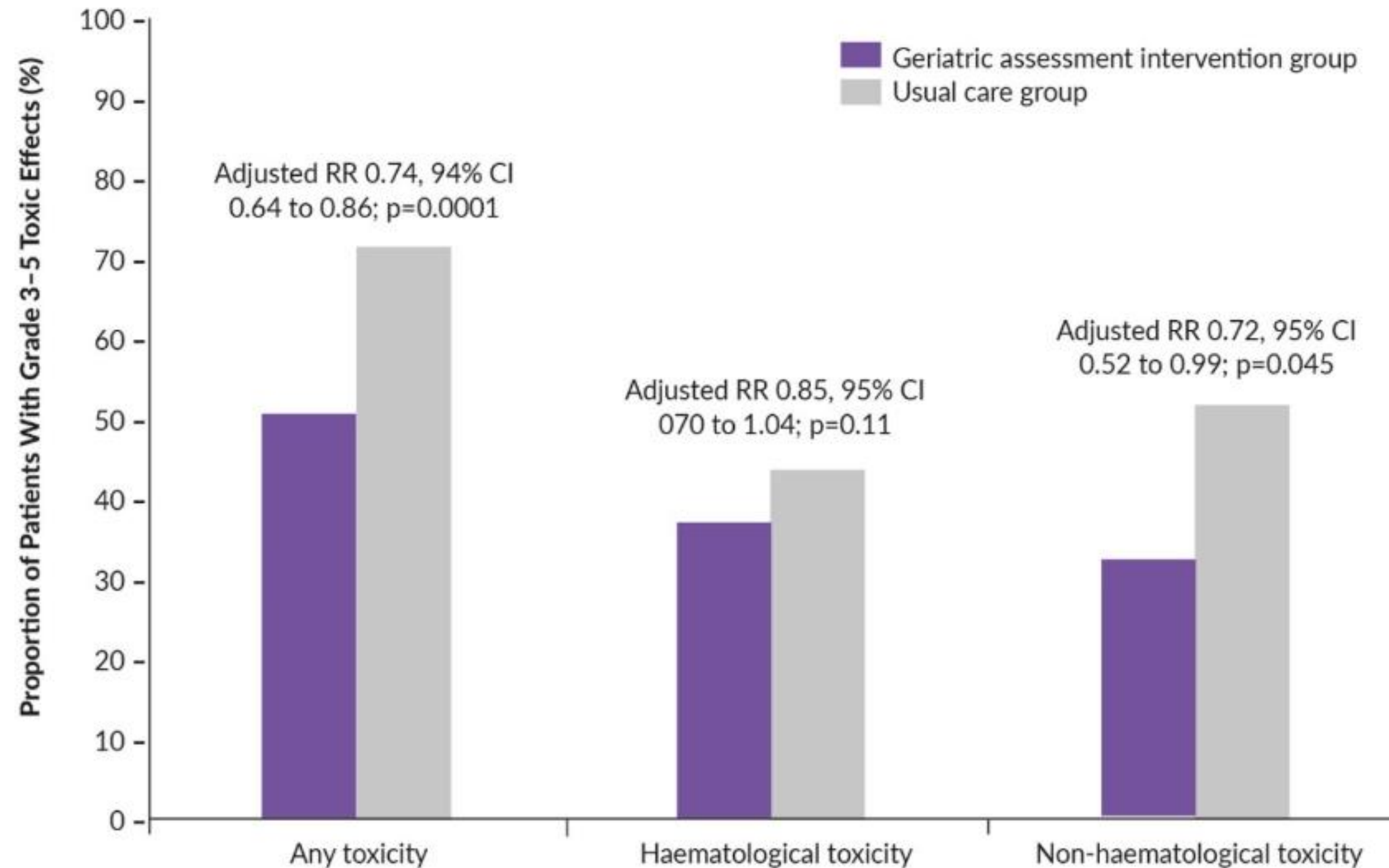


Epidemiology and Current Challenges:

Figure 3 Overall Survival Curves according to Intensity of Treatment ($P = .003$) (A) and Cytogenetic Risk Groups ($P = .114$) (B)



Prevalence of grade ≥ 3 toxicity over 3 months with or without geriatric assessment intervention



Key Factors Affecting AML in Elderly Patients

1. Different Biology

- Higher prevalence of secondary AML from MDS/MPN
- Increased mutations in *TP53*, *ASXL1*, *RUNX1*
- Clonal hematopoiesis leads to poor prognosis

2. Unfavorable Cytogenetics

- Increased frequency of complex karyotype, Monosomal karyotype, -5/del(5q), -7/del(7q)

3. Decline in Performance Status

- Reduced organ function affects chemotherapy tolerance
- Poor ECOG/ Karnofsky score limits intensive treatment options

4. Acquired Comorbidities

- Cardiovascular disease, renal dysfunction, diabetes
- Increased treatment-related toxicities and mortality

Challenges in Assessing and Treating Elderly

- **Historical Reliance on Age and Performance Status**
 - Treatment decisions traditionally based on chronological age
 - ECOG/Karnofsky scores historically used to determine eligibility
- **Limitations of Using Age Alone**
 - Age is a poor standalone predictor of treatment tolerance
 - Biological and functional age often differ significantly

Aim of assessing the fitness of older patients with AML

They are candidates for curative therapy that can achieve a durable CR.

This thorough evaluation is intended to rule out treatments that might

- 1. exacerbate age-related frailties**
- 2. induce organ damage due to previous or current comorbidities**
- 3. be difficult for the patient to adhere to because of their individual characteristics in order to reduce treatment-related mortality**

Challenges in Assessing and Treating Elderly

- **Definition of "Fitness" vs "Frailty"**
 - **Fitness**: physiological resilience and ability to tolerate intensive therapy
 - **Unfitness**: limited function to receive intensive therapy, should be treated with non-intensive therapy
 - **Frailty**: functional decline, comorbidities, and reduced physiological reserve
- **Importance of Comprehensive Assessment**
 - Use of geriatric assessment tools to evaluate cognition, comorbidities, nutrition, and physical function
 - Helps tailor treatment decisions for better outcomes

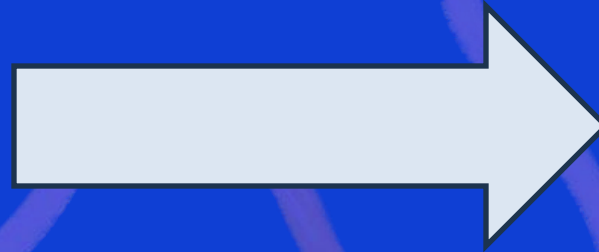
Comprehensive Geriatric Assessment (CGA)

- Elderly patients with acute leukemia (AML and ALL) often have multiple comorbidities, reduced physiological reserves, and increased vulnerability to treatment-related toxicities.
- Comprehensive Geriatric Assessment (CGA) plays a crucial role in evaluating their overall health status, guiding treatment decisions, and predicting clinical outcomes.

Geriatric Assessment



Screening for Frailty



**Comprehensive Geriatric
Assessment**

Step 1: Screening for Frailty

Common Frailty Screening Tools:

- **Geriatric 8 (G8 Score)**
 - **Score < 14 → Indicates potential frailty → CGA is recommended**
- **Clinical Frailty Scale (CFS)**
 - **Score ≥ 5 → Indicates frailty**
- **Fried Frailty Criteria (≥ 3 criteria)**
 - **Weakness, Weight loss, Exhaustion, Slowness, Low activity**

 **If frailty is detected → CGA is recommended**

 **If not frail → Intensive chemotherapy may be considered**

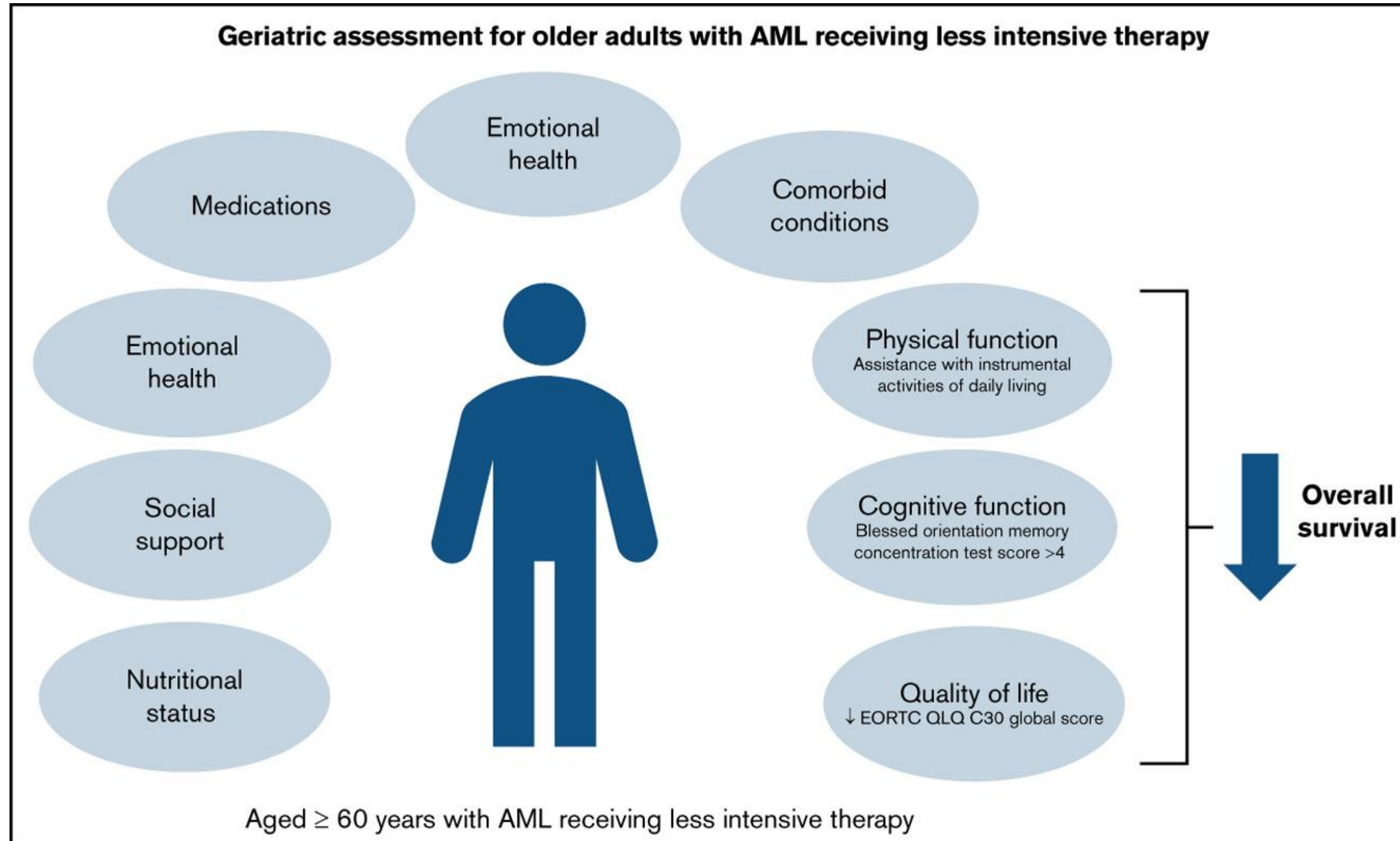
Step 1: Screening for Frailty

Question	Response Options	Score
Food intake (compared to usual)	Severe decrease	0
	Moderate decrease	1
	No change	2
Weight loss in the past 3 months	> 3 kg	0
	1–3 kg	1
	No weight loss	2
Mobility	Bedridden	0
	Can sit but unable to walk	1
	Can move independently	2
Neuropsychological problems	Severe dementia/depression	0
	Mild cognitive issues	1
	No problems	2
Body Mass Index (BMI)	< 19 kg/m ²	0
	19–21 kg/m ²	1
	> 21 kg/m ²	2
Polypharmacy (number of medications)	≥ 3 medications	0
	< 3 medications	1
Self-perceived health status	Very poor	0
	Poor	1
	Good/excellent	2
Age	≥ 85 years	0
	80–84 years	1
	< 80 years	2

Interpretation: Geriatric 8 (G8 Score)

- Total Score < 14 → Frailty → **Perform CGA**
- Total Score ≥ 14 → No significant frailty

Step 2: Comprehensive Geriatric Assessment



Geriatric Assessment (ASCO 2023 Guidelines)

- **Physical Function**

- Activities of daily living (ADLs) and instrumental ADLs
- Gait speed and fall risk assessment
- Performance status (ECOG/KPS)
- Short Physical Performance Battery (SPPB)

- **Cognitive Function**

- Screening tools: Mini-Cog, MoCA, MMSE
- Assessment of dementia and delirium risk



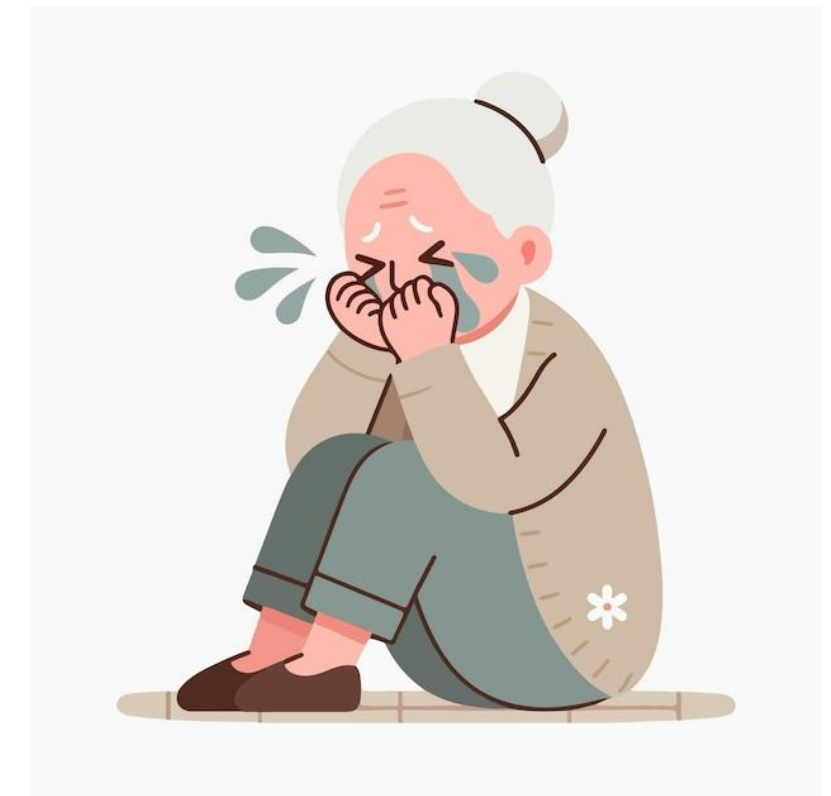
Geriatric Assessment (ASCO 2023 Guidelines)

- **Emotional Health**

- Screening for depression and anxiety
- Geriatric Depression Scale (GDS) and PHQ-9

- **Comorbid Conditions**

- Charlson Comorbidity Index
- Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI)
- Impact on treatment tolerance and prognosis



Geriatric Assessment (ASCO 2023 Guidelines)

- **Polypharmacy**

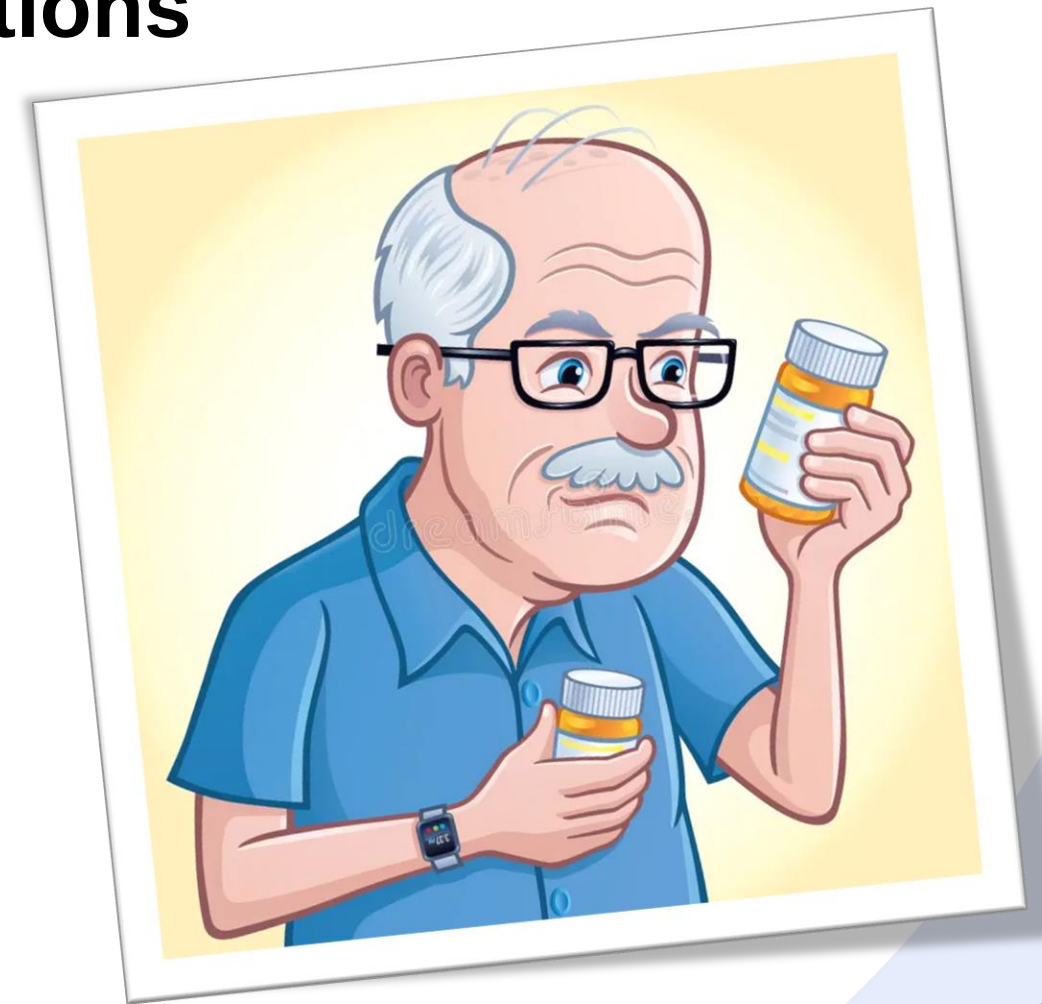
- Medication review to reduce inappropriate prescriptions
- Consideration of drug-drug interactions
- Assessment of social determinants of health

- **Nutrition**

- Malnutrition screening (MUST, MNA)
- Impact on chemotherapy tolerance and outcomes

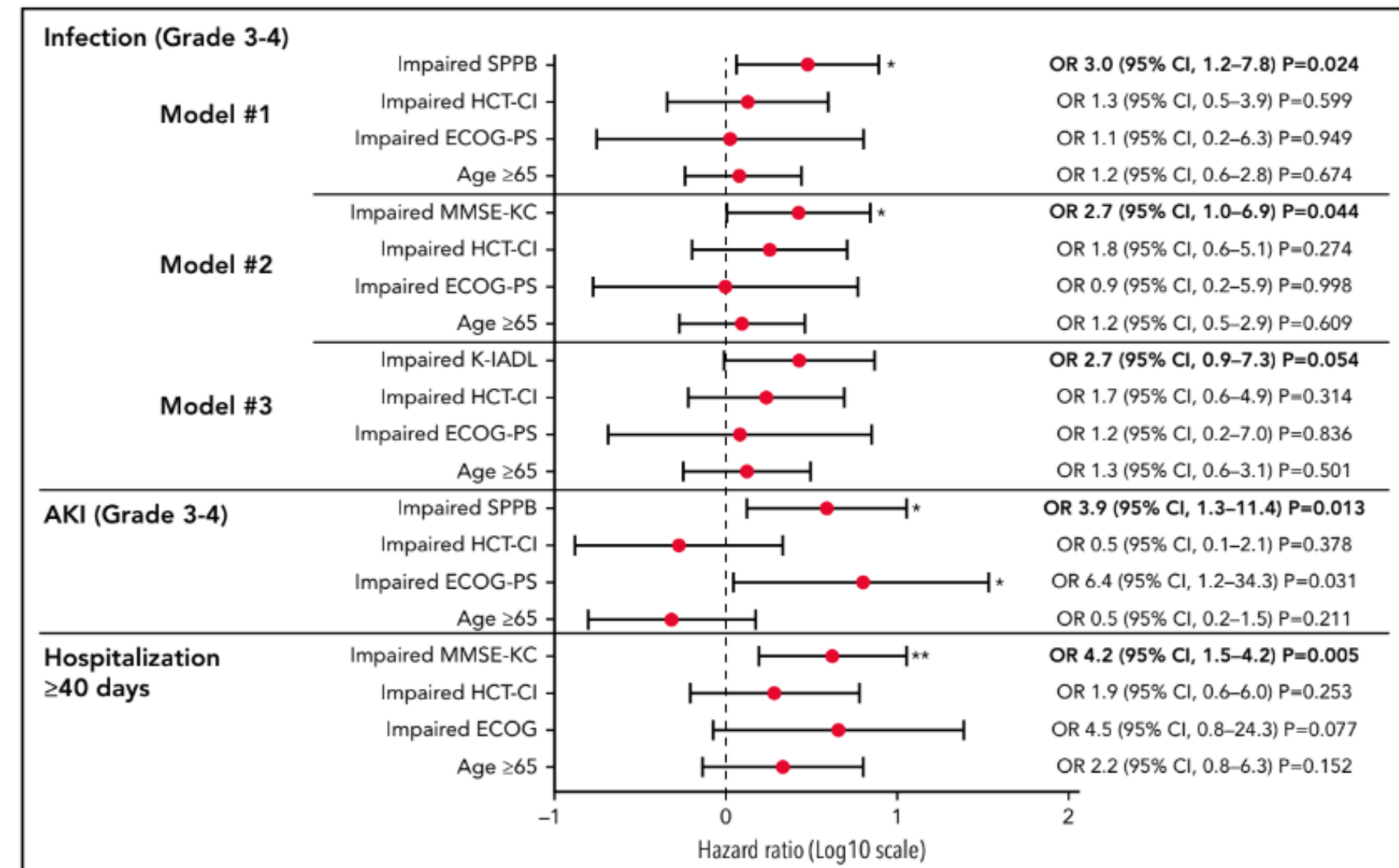
- **Social Support**

- Caregiver availability and support systems (MOS social support 8 item)
- Assessment of social determinants of health



Geriatric assessment predicts nonfatal toxicities and survival for intensively treated older adults with AML (N=105)

Characteristic	No.	%	Median (range)
Age at diagnosis, y			64 (60-75)
60-64	54	51.4	
65-70	37	35.3	
71-75	14	13.3	
Sex			
Male	65	61.9	
Female	40	38.1	
AML disease type			
De novo	73	69.5	
Secondary	32	30.5	
ELN 2017 criteria			
Favorable	24	22.9	
Intermediate	49	46.7	
Poor	32	30.5	
Genetic mutation			
Biallelic CEBPA	6	5.7	
NPM1 without FLT3-ITD or with FLT3-ITD (low)	13	12.4	
NPM1 with FLT3-ITD (high)	10	9.5	
FLT3-ITD (high) without NPM1	9	8.6	
RUNX1	10	9.5	
ASXL1	9	8.6	
TP53	2	1.9	



Physical Function Impact (Blood 2022)

- **Short Physical Performance Battery (SPPB) is used to assess physical function in older patients.**
- **Study Findings:**
 - Lower SPPB scores → Higher risk of Grade 3-4 infections ($P = .024$).
 - Acute renal failure ($P = .013$) → Correlated with decreased physical performance
 - OS outcomes → Patients with lower SPPB scores had reduced survival rates
- **Clinical Implication:**
 - SPPB should be assessed before chemotherapy
 - Physical rehabilitation programs may improve outcomes

Geriatric assessment for older adults receiving less-intensive therapy for AML: report of CALGB 361101

- CALGB 11002 was a phase 2 randomized study of adults > 60 years with newly diagnosed AML, testing the safety and efficacy of adding bortezomib to a 10-day decitabine regimen vs decitabine alone

Baseline characteristics	Median (range) or frequency (%)
Demographics	
Age (years) median (range)	72.7 (60.6-92.4)
% 60-64	14.6
% 65-69	19.8
% 70-74	24.0
% 75-79	20.8
% ≥80	20.8
% female	30.2
% white	90.6
% non-Hispanic	91.7
% ECOG performance status ≤1	73.9
Clinical onset of AML	
% De novo	63.2
% Therapy-related	11.6
% MDS/AHD	25.2
ELN classification	
% Normal	27.4
% Intermediate-II	22.1
% Adverse	38.9
% No diagnosis cytogenetics	11.6

Table 3. Multivariate analysis of baseline assessment, geriatric assessment measures, and mortality

Characteristic	Hazard ratio* (95% confidence interval)	P value
Mortality		
HCT-CI		
Reference: 0		
1-2	1.8 (0.8-3.8)	.152
≥3	2.5 (1.2-5.2)	.018
BOMC test score		
Reference: < 4		
≥4	1.7 (1-2.8)	.048
EORTC global health score	0.99 (0.9-1)	.050
6-Month Mortality (odds ratio)		
IADL (subscale of the OARS)		
Reference: 14		
<14	3.5 (1.2-10.4)	.025
BOMC test score		
Reference: < 4		
≥4	3.14 (1.1-8.6)	.026

OARS, Older Americans Resources and Services.

*Adjusted for age, physician-rated Karnofsky Performance Status, and treatment arm.

Cognitive Function and Treatment Outcomes

- **Cognitive function plays a key role in treatment-related complications.**
- **Key Associations:**
 - **Grade 3-4 infections → More common in patients with cognitive impairment.**
 - **Prolonged hospitalization (≥ 40 days) → Patients with cognitive deficits tend to have extended hospital stays.**
 - **Delirium development during treatment → Cognitive impairment increases delirium risk, affecting recovery.**
- **Clinical Implication:**
 - **Cognitive screening should be conducted before treatment**
 - **Geriatric support programs may help manage risks.**

Dale W, Klepin HD, Williams GR, et al. J Clin Oncol. 2023;41(25):2528-2548.

Cancer and Aging Research Group. New 2023 ASCO Geriatric Oncology Updated Guidelines. 2023.

Mohile SG, Magnuson A, Pandya C, et al. Geriatric assessment-guided care processes for older adults: ASCO recommendations.

Depression and Survival Outcomes

- **Geriatric Depression Scale-Short Form (SGDS-K) is used to assess depression in older patients.**
- **Higher SGDS-K scores are associated with:**
 - **Reduced OS → Depressed patients tend to have lower survival rates.**
 - **Increased Risk of MDD → Negatively impacts quality of life and treatment adherence.**
 - **Worse Treatment Outcomes → Depression correlates with poor response to treatment.**
- **Clinical Implication:**
 - **Depression screening should be included in the geriatric assessment.**
 - **Psychological support and behavioral therapy should be considered.**

Geriatric Assessment in Hematology (the GAH scale)

GAH score >6
appeared
predictive of
inferior
survival

Table 1 – Dimensions used for the development of the GAH scale.

Dimension	Measurement	Range of score	Cut-off point (1 point)
No. of drugs	Medication count of drugs of current use.	Continuous	$\geq 5^{17}$
Gait speed	Double determination of gait speed at usual pace over a 4 meter course ^{19,20}	Continuous	$< 0.8 \text{ m/s}^{21}$
Mood	Single item from the CES-D ²² : <i>In the last week, did you feel depressed?</i>	Never, rarely, or occasionally (no more than 2 days); frequently, most of the time or all time (3–7 days)	Frequently, most of the time or all time (3–7 days)
Activities of daily living	- Item no. 4 of the VES-13 Instrument²⁴: <i>Do you have any difficulty in ...?</i> - Do you need any help in your daily living? - Do you have a caregiver?	Yes/no	Needs help in at least one area
Subjective health status	Single item from the VES-13 Instrument ²⁴ : <i>Compared to other people your age, would you say your health is...?</i>	Poor, fair, good, very good, or excellent	Poor and fair
Nutrition	Four items from the MNA-SF ³⁰ : BMI, weight loss during the last 3 months, food intake decline over the past 3 months, and psychological stress or acute disease.	0–10	≤ 8
Mental status	SPMSQ ³¹	Right/wrong	≥ 3 errors
Comorbidities	Prognostic Index for 4-year Mortality in Older Adults ³⁵	0, for absence; 1 point for DM or BMI $< 25 \text{ kg/m}^2$; 2 points for cancer, lung disease, heart failure, or smoking habit.	≥ 3

Abbreviations: BMI, body mass index; CES-D, Centre for Epidemiological Studies Depression Scale; DM, diabetes mellitus; MNA-SF, Mini-Nutritional Assessment questionnaire; SPMSQ, Short Portable Mental Status Questionnaire; VES-13, 13-item Vulnerable Elders Survey.

Evidence from Recent Studies (ASCO 2023)

- **ASCO 2023 guidelines emphasize the use of Geriatric Assessment to predict risks and outcomes in older adults receiving cancer treatment.**
- **Recent studies indicate that Physical Function, Cognitive Function, and Depression significantly impact cancer treatment outcomes.**
- **Key Findings:**
 - **Physical Function → Predicts the risk of complications**
 - **Cognitive Function → Associated with infections and prolonged hospitalization**
 - **Depression → Impacts survival and treatment outcomes**

Treatment Decision Making: Using GA to Guide Therapy

Impact on Treatment Selection

- GA helps guide:
 - Standard vs. reduced-intensity therapy → Based on physical and cognitive status.
 - Choice of therapy → Chemotherapy, targeted therapy, or supportive care.
 - Patient-centered care → Aligns treatment with patient goals and life expectancy.
- Clinical Example:
 - Frail patients may benefit from dose-reduced regimens or alternative therapies.

Treatment Decision Making: Using GA to Guide Therapy

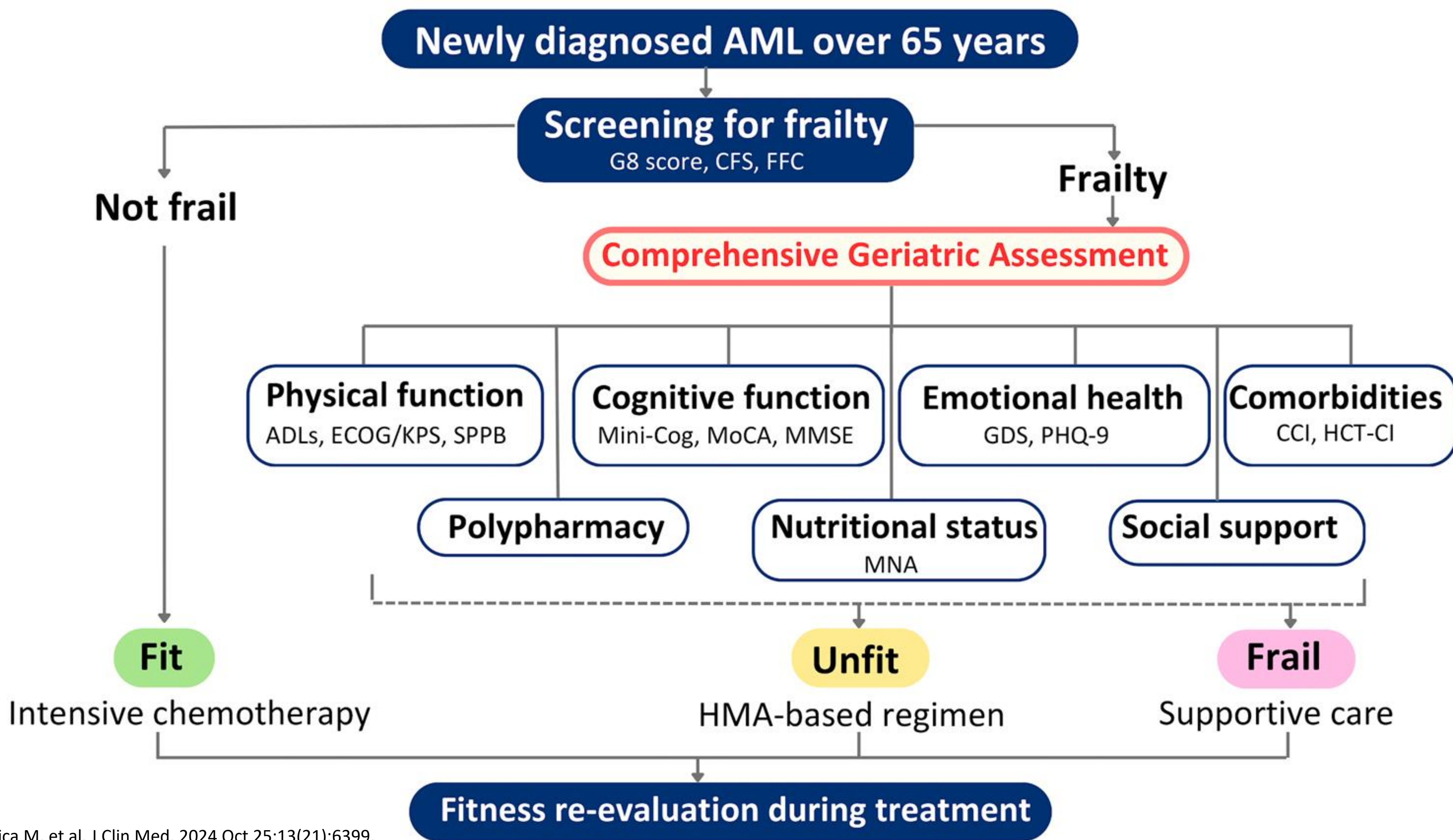
Dose Modifications & Supportive Care Needs

- Dose Modifications:
 - Adjusts chemotherapy dose to reduce severe toxicities.
 - Prevents Grade 3-4 toxicities such as neutropenia, renal failure, and infections.
- Supportive Care Needs:
 - Identifies need for nutritional, physical therapy, and psychosocial support.
 - Addresses polypharmacy and comorbidities for better treatment tolerance.
 - Early integration of palliative care in high-risk patients.

Treatment Decision Making: Using GA to Guide Therapy

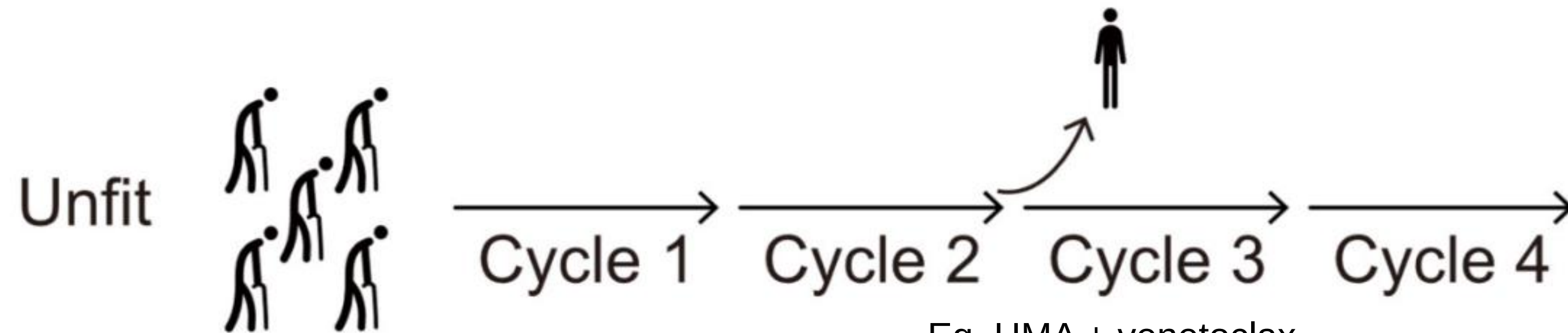
Monitoring & Predictive Value of GA

- Monitoring Requirements:
 - Determines follow-up frequency and reassessment schedule.
 - Helps predict hospitalization, dose adjustments, and treatment interruptions.
 - Guides proactive interventions to prevent complications.
- Predictive Value of GA:
 - Treatment Toxicity: GA predicts chemotherapy-related side effects.
 - Early Mortality: Identifies frail patients at higher risk of early death.
 - Overall Survival: Better GA scores correlate with improved survival rates.

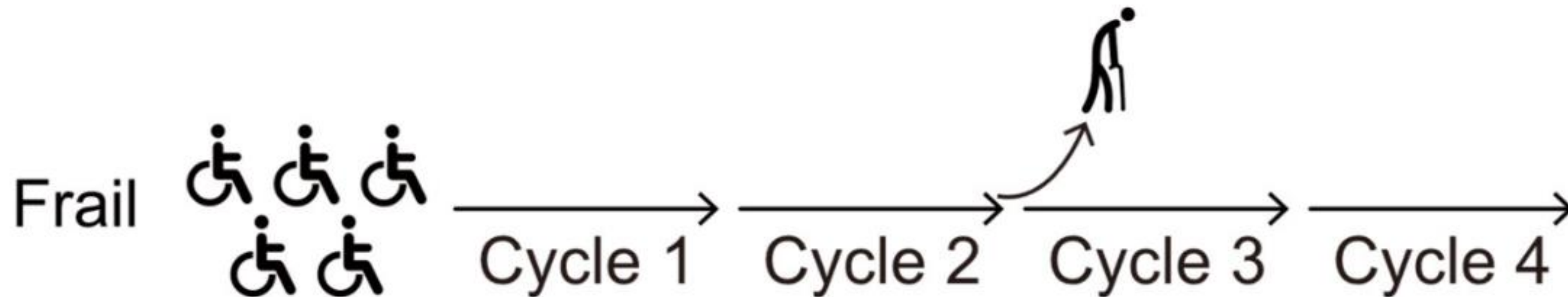


Frailty is a dynamic risk factor

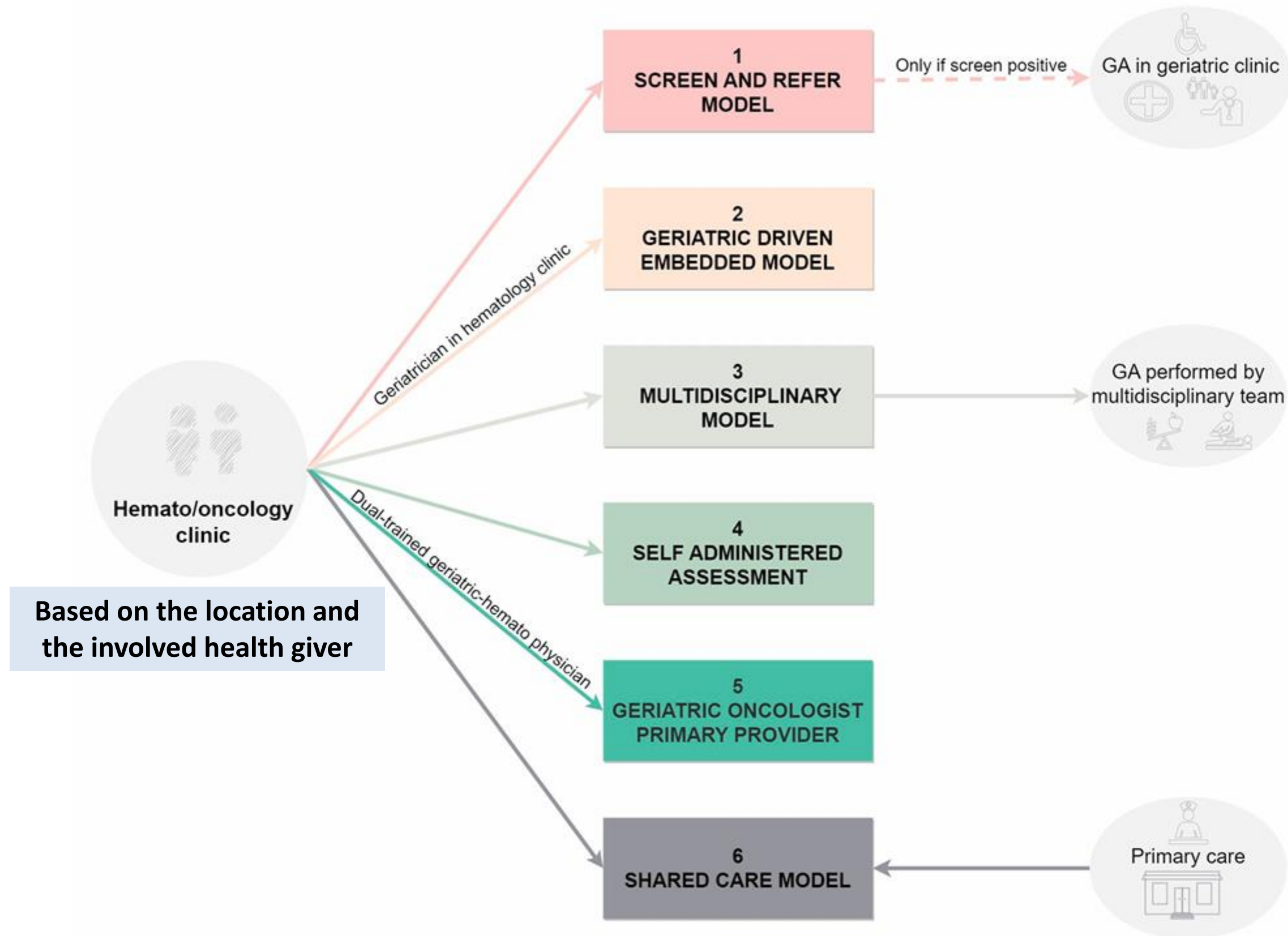
Eg. Allogeneic SCT in non-favorable risk



Eg. HMA + venetoclax



Models of comprehensive geriatric assessment



Future Directions in Geriatric Assessment

- **Areas for Development:** Enhancing GA tools for better predictive value.
- **Integration with Novel Therapies:** Applying GA to immunotherapy, targeted therapy, and emerging cancer treatments.
- **Role in Non-Intensive Treatment:** Expanding GA use in palliative and supportive care settings.

CONCLUSION

- **Comprehensive Geriatric Assessment (CGA) is essential for optimizing cancer care in older adults.**
- **GA helps identify risks, personalize treatment, and improve clinical outcomes.**
- **Key Benefits of GA:**
 - **Reduces treatment toxicity and complications.**
 - **Enhances quality of life and functional independence.**
 - **Supports informed decision-making and tailored supportive care.**
- **Next Steps:**
 - **Expand GA integration into routine hemato-oncology practice.**
 - **Encourage interdisciplinary collaboration for improved patient care.**
 - **Continue research on GA's role in emerging cancer therapies.**

THANK
YOU