VOLUME 32 · NUMBER 24 · AUGUST 20 2014

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

International Society of Geriatric Oncology Consensus on Geriatric Assessment in Older Patients With Cancer

Hans Wildiers, Pieter Heeren, Martine Puts, Eva Topinkova, Maryska L.G. Janssen-Heijnen, Martine Extermann, Claire Falandry, Andrew Artz, Etienne Brain, Giuseppe Colloca, Johan Flamaing, Theodora Karnakis, Cindy Kenis, Riccardo A. Audisio, Supriya Mohile, Lazzaro Repetto, Barbara Van Leeuwen, Koen Milisen, and Arti Hurria

Hans Wildiers, Pieter Heeren, Johan Flamaing, Cindy Kenis, and Koen Milisen, University Hospitals Leuven, KU Leuven, Leuven, Leuven, Belgium; Martine Puts, University of Toronto, Toronto, Ontario, Canada; Eva Topinkova, Charles University, Prague, Czech Republic; Maryska L.G. Janssen-Heijnen, VieCuri Medical Centre, Venlo, and Maastricht University Medical Center, Maastricht; Barbara Van Leeuwen, Groningen University, Groningen, the Netherlands; Martine Extermann, University of South Florida, Tampa, FL; Claire Falandry, Lyon University, Pierre-Bénite; Etienne Brain, Hôpital René Huguenin–Institut Curie, Saint-Cloud, France; Andrew Artz, University of Chicago, Chicago, IL; Giuseppe Colloca, Catholic University of Sacred Heart, Rome; Lazzaro Repetto, G. Borea Hospital, Sanremo, Italy; Theodora Karnakis, University of Sao Paulo Medical School, Sao Paulo, Brazil; Riccardo A. Audisio, University of Liverpool, Liverpool, United Kingdom; Supriya Mohile, University of Rochester, Rochester, NY; and Arti Hurria, City of Hope, Duarte, CA.

Published online ahead of print at www.jco.org on July 28, 2014.

Supported in part by the Belgian Cancer Plan (2012-2015) and Grant No. KPC 24 B 026 from the Belgian Federal Public Service of Health, Food Chain Safety and Environment.

H.W. and P.H. contributed equally to this work.

Presented at the 13th Annual Conference of the International Society of Geriatric Oncology, Copenhagen, Denmark, October 24-26, 2013.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Corresponding author: Hans Wildiers, MD, PhD, Department General Medical Oncology, University Hospitals Leuven, Herestraat 49, 3000 Leuven, Belgium; e-mail: hans.wildiers@uzleuven.be.

0732-183X/14/3224w-2595w/$20.00

DOI: 10.1200/JCO.2013.54.8347

ABSTRACT

Purpose
To update the International Society of Geriatric Oncology (SIOG) 2005 recommendations on geriatric assessment (GA) in older patients with cancer.

Methods
SIOG composed a panel with expertise in geriatric oncology to develop consensus statements after literature review of key evidence on the following topics: rationale for performing GA; findings from a GA performed in geriatric oncology patients; ability of GA to predict oncology treatment–related complications; association between GA findings and overall survival (OS); impact of GA findings on oncology treatment decisions; composition of a GA, including domains and tools; and methods for implementing GA in clinical care.

Results
GA can be valuable in oncology practice for following reasons: detection of impairment not identified in routine history or physical examination, ability to predict severe treatment-related toxicity, ability to predict OS in a variety of tumors and treatment settings, and ability to influence treatment choice and intensity. The panel recommended that the following domains be evaluated in a GA: functional status, comorbidity, cognition, mental health status, fatigue, social status and support, nutrition, and presence of geriatric syndromes. Although several combinations of tools and various models are available for implementation of GA in oncology practice, the expert panel could not endorse one over another.

Conclusion
There is mounting data regarding the utility of GA in oncology practice; however, additional research is needed to continue to strengthen the evidence base.

J Clin Oncol 32:2595-2603. © 2014 by American Society of Clinical Oncology

INTRODUCTION

More than half of patients newly diagnosed with cancer are age ≥ 65 years.[1] Although this number is expected to increase as the world population ages, there is less evidence on which to base treatment decisions for older patients with cancer, because this group is underrepresented in clinical trials.[2] Furthermore, there is heterogeneity in the aging process, which further contributes to the complexity of treatment decisions. These factors contribute to age-related variations in treatment patterns and outcomes, potentially resulting in increased likelihood of under- or overtreatment, which can influence both risk of treatment toxicity and survival.[3,4] Because chronologic age alone is a poor descriptor of heterogeneity in the aging process, a systematic and evidence-based way of describing the heterogeneity is needed to guide oncology treatment decisions. A comprehensive geriatric assessment (CGA) can fill this knowledge gap.[5,6] CGA is defined as a multidimensional, interdisciplinary diagnostic process focusing on determining an older person's medical, psychosocial, and functional capabilities to develop a coordinated and integrated plan for treatment and long-term follow-up.[7] In the general (nononcologic) geriatric population, CGA-guided treatment plans have been shown in some, but not all, studies to improve overall survival (OS), quality of life, and physical function and decrease the risk of hospitalization and nursing home placement.[8-10] However, these benefits have primarily been noted in acute geriatric care units.[8,11] Data on the utility of GA in the older (often ambulatory) cancer population have emerged only more recently.[12] Because CGA research specifically in the oncology setting has

mainly studied the diagnostic process/assessment and has not yet thoroughly focused on geriatric interventions, we decided to use the term geriatric assessment (GA) rather than CGA.

The International Society of Geriatric Oncology (SIOG) established recommendations on GA in older patients with cancer in 2005.[13] Numerous publications have emerged during the subsequent years. To synthesize this evidence and provide consensus opinion from individuals with expertise in geriatric oncology, SIOG established four multidisciplinary task forces consisting of individuals with international expertise in CGA in oncology practice. The aim of this article is to synthesize the evidence and provide geriatric oncology consensus on key questions on GA in geriatric oncology: (1) What is the rationale for performing GA? (2) What information is provided by a GA beyond that captured in a standard history and physical exam? (3) What is the ability of GA to predict oncology treatment–related complications? (4) What is the association between GA findings and OS? (5) What is the impact of GA findings on oncology treatment decisions? (6) What should a GA comprise, including domains and tools? (7) How should GA be organized and implemented in clinical care?

METHODS

A review by Puts et al,[12] relevant to questions 2 to 5, which included published or in-press data through November 16, 2010, was considered as the starting point for our review. Retrieved articles from a systematic literature search by P.H. (Appendix Table A1, online only, provides detailed information on methodology) were interpreted and discussed by the multidisciplinary group of experts, who could add relevant publications.

A quality score of the retrieved studies was performed by P.H. and C.K. using the methodologic index for nonrandomized studies (Appendix, online only).[14] After a first draft by the writing team, seven expert workgroups (for seven questions) were created (Appendix, online only). For all recommendations, data from the review by Puts et al,[12] as well as the newly selected publications, were used. Table 1 and Appendix Tables A2 to A6 (online only) list the recent publications; the review by Puts et al provided the older data. Finally, a task group consensus was developed. The Oxford 2011 levels of evidence (Appendix Table A7, online only) were used to grade the quality of evidence and strength of recommendations.[15]

RESULTS

Question 1

What is the rationale for performing GA?

Key evidence. GA can fill a significant knowledge gap, as described in the Introduction. Many publications have made statements on the rationale for performing GA in older patients with cancer. Key concepts are summarized in the Appendix Table A2 (online only), and most of these concepts are discussed in more detail in the questions 2 to 5 of this article.

Interpretation of key evidence. Important reasons to perform GA in older patients with cancer are: detection of unidentified problems and risks for which targeted interventions can be applied (question 2); prediction of adverse outcomes (eg, toxicity, other relevant items such as functional or cognitive decline, postoperative complications; question 3); and better estimation of residual life expectancy and lethality of the malignancy in the context of competing comorbidities and general health problems (question 4; level 5).

The main goal of GA is to provide a comprehensive health appraisal to guide targeted geriatric interventions and appropriate cancer treatment selection (question 5). GA has the potential to evaluate the balance of benefits and harms of performing or omitting specific oncologic interventions (level 5).

Which patients would benefit from GA is an area of controversy. Many oncologic studies have used age $\geq$ 70 years as the age for implementing GA, but other age cutoffs have been proposed. An active area of research is to identify whether a shorter geriatric screening tool can identify which older patients with cancer would benefit from more comprehensive GA (level 5).

Question 2

What information is provided by a GA beyond that captured in a standard history and physical exam?

Key evidence. The literature from 2010 to 2013 was reviewed to identify research studies summarizing the findings from GA performed in an oncology patient population. A comprehensive review of these study findings is summarized in the Appendix Table A3 (online only). Literature from previous years is summarized in an article by Puts et al.[12]

GA identifies age-related problems not typically identified by a routine history and physical examination in approximately half of older patients with cancer.[16,17] Only one (large) study[15] reported the percentage of patients per domain in whom GA had identified new problems, with the most frequent problems being fatigue (36.6%), nutritional issues (37.6%), and functional impairments (40.1%). Several studies reported only the percentage of patients with at least one deficit, with percentages varying between 90.4% and 92.6%.[24,32] Comparison of the different studies is difficult because of the use of different populations, regions, tools, and cutoffs.

Interpretation of key evidence. Deficits in GA domains are frequent in older patients with cancer (level 3). Assessment of all domains is relevant because GA can potentially identify deficits across domains (level 3). GA reveals deficits that are not routinely captured in a standard history and physical examination (level 3).

Question 3

What is the ability of GA to predict oncology treatment–related complications?

Key evidence. GA has the potential to predict several relevant treatment-related complications (eg, postoperative complications, toxicity related to systematic treatment, and so on; Appendix Table A4, online only).[12,19,25,39-42] Because newfound articles on this topic (not discussed in Puts et al[12] review) only focused on severe toxicity (generally defined as grade 3 to 5 adverse events[43]) related to systemic treatments, we refer to the Puts et al review for predictive capabilities of GA for other outcomes.

Most previously published studies on prediction of chemotherapy toxicity were retrospective, small in size, and underpowered to discover clinically relevant changes.[12] Some studies found no predictive value of GA variables for treatment toxicities, whereas other studies did. Two large prospective studies—CARG (Cancer and Aging Research Group)[20] and CRASH (Chemotherapy Risk Assessment Scale for High-Age Patients)[41]—clearly identified parameters of GA capable of predicting severe chemotherapy-related complications in a heterogeneous cancer population. Both studies attempted to correct for differences in treatment characteristics (CRASH: MAX-2 index;

Table 1. Domains and Instruments Used in GA*

Domain	Tool
Demographic data and social status	Questions on living situation, marital status, educational level, safety of environment, financial resources[15-18]
	MOS Social Activity Survey[19-21]
	Caregiver burden[22]
	MOS Social Support Survey (Emotional/Information and Tangible Subscales)[19-21]
	Summary of some criteria (eg, availability of family support, appropriateness of social environment)[16,17,23,24]
Comorbidity	Charlson comorbidity index[18,23,24,25,26,27]
	CIRS[28,29]
	CIRS-G[16,17,29-31]
	NYHA[31]
	No. of comorbid conditions[21]
	Simplified comorbidity score[24]
	Summary of comorbidities[16]
	Hematopoietic cell transplantation comorbidity index[32]
	Physical Health Section (subscale of OARS)[19,20]
Functional status	ADLs (Katz index)[15-17,22-24,27,30-33]
	IADLs (Lawton scale)[15,17,22-24,26,27,31-33]
	PS index[27]
	Barthel index (any version)[25,28]
	Lawton-Brody IADL Scale[25]
	Nottingham Extended ADL Scale[28]
	ADLs (subscale of MOS Physical Health)[20,21]
	IADLs (subscale of OARS)[19-21]
	Pepper assessment tool for disability[32]
	Visual and/or hearing impairment, regardless of use of glasses or hearing aids[17,22,23,]
	MOS Physical Health (any version)[18,19]
	Mobility problem (requiring help or use of walking aid)[22]
	Timed Get Up and Go[16,19,20,26,27,33]
	Hand grip strength[32]
	Short Physical Performance Battery[32]
	One-leg standing balance test[16,27]
	Walking problems, gait assessment, and gait speed[16,17,23]
	ECOG PS[23,25,26]
	Karnofsky self-reported performance rating scale[19-21]
	Karnofsky health care professional-rated performance rating scale[19-21]
Cognition	Mini Mental State Examination (any version)[15-17,23-28,30,31,33,34]
	Informant Questionnaire on Cognitive Decline in the Elderly (any version)[22,34]
	Modified Mini Mental State Examination[32]
	Clock-drawing test[23,26]
	Blessed Orientation-Memory-Concentration Test[19,20]
Depression	Geriatric Depression Scale (any version)[15-17,22-29,31,33]
	Center for Epidemiologic Studies Depression Scale[32]
	Hospital Anxiety and Depression Scale[19,20]
	Mental health index[18]
	Presence of depression (as geriatric syndrome)[30]
	Distress thermometer[32]
Nutrition	Body-mass index (weight and height)[16-23,26]
	Weight loss (unintentional loss in 3 or 6 months)[16,17,19-21,23,24]
	Mini Nutritional Assessment (any version)[15,16,25,27,28,33,34]
	Short Nutritional Assessment Questionnaire[22]
	DETERMINE Nutritional Index[26]
Fatigue	MOB-T[15]
Polypharmacy	Beers criteria[35]†
	STOPP and START criteria[36]†
Geriatric syndromes‡	Dementia[24,26,29,30]
	Delirium[24,26,29,30]
	Incontinence (fecal and/or urinary)[16,17,22-24,26,29,30]
	Osteoporosis or spontaneous fractures[22,24,26,29,30]
	Neglect or abuse[24,26,29,30]
	Failure to thrive[26,29]

(continued on following page)

Table 1. Domains and Instruments Used in GA* (continued)

Domain	Tool
	Self-reported No. of falls (within different time frames)[15-17,19-23,26,27,29,30]
	Constipation[22]
	Polypharmacy[15-17,19,22,23,26,28]
	Pressure ulcus[22]
	Sarcopenia[37]†

Abbreviations: ADL, activity of daily living; CIRS, Cumulative Illness Rating Scale; CIRS-G, Cumulative Illness Rating Scale-Geriatrics; DETERMINE, Disease, Eating poorly, Tooth loss/mouth pain, Economic hardship, Reduced social contact, Multiple medicines, Involuntary weight loss/gain, Needs assistance in self-care, Elder years > 80; ECOG, Eastern Cooperative Oncology Group; GA, geriatric assessment; IADL, instrumental activity of daily living; MOB-T, Mobility Tiredness Test; MOS, Medical Outcomes Study; NYHA, New York Heart Association; OARS, Older Americans Resources and Services; PS, performance status; START, Screening Tool to Alert Doctors to Right Treatment; STOPP, Screening Tool of Older Person's Prescriptions.

*For studies published before November 16, 2010, see review by Puts et al.[12]

†Although this tool was not used in newfound articles, it is mentioned because of high relevance in geriatrics.

‡Some studies reported geriatric syndromes that overlap with other domains.

CARG: poly- *v* monochemotherapy and standard *v* reduced dose), but these categorizations do not fully capture the diversity of specific chemotherapy drugs and schedules. The predictive ability of these models remains moderate at the individual level, and they require further validation and optimization.

Aparicio et al[39] and Falandry et al[42] studied more-homogenous populations of patients with untreated metastatic colorectal cancer and patients with metastatic breast cancer who received first-line chemotherapy, respectively. The specific GA variables predictive for toxicity differed in most studies; however, the factors most consistently associated with toxicity were functional status[12,25,41] and comorbidity.[12] Other identified risk factors were cognitive problems,[12,39,41] lack of social support,[12] hearing difficulties,[20] falls,[20] nutritional status,[41] poor grip strength,[12] and GA group allocation (ie, fit, vulnerable, or frail).[12]

Interpretation of key evidence. GA items are predictive (independent from classic oncologic predictors) of the risk of severe treatment-related toxicity in a variety of diseases and treatment settings (level 3). The optimal geriatric parameters (including cutoff points) to predict severe treatment toxicity or modify therapeutic approach (including dose or regimen adaptations and/or GA-guided interventions to decrease risk of toxicity) have not yet been established for different cancer types or treatment options (level 4).

Question 4

What is the association between GA findings and OS?

Key evidence. There is emerging evidence in the literature regarding the association between factors captured in GA and OS, with several new studies from 2010 to 2013 (Appendix Table A5, online only). However, a majority of studies were small in size (< 100 patients) and/or included patients with heterogeneous diseases, treatments, and tumor stages, which could independently have had an impact on overall mortality. Most, but not all, studies identified geriatric parameters that were independent predictors of mortality.[12,22,44-44b] Besides age strata, factors most consistently associated with OS were functional status,[12,24,26] nutritional status,[12,24,26,33,34] overall fitness,[12,28,30,31] and mental health.[12,24,26] Most studies performed multivariable analyses correcting for some general aspects, but the generally heterogeneous populations in terms of oncologic prognosis (independent of age) were a major weakness. Prognostic models based on GA parameters have been developed in the general geriatric population (eg, Lee score,[45] Porock scale,[46] and other scales available at the Eprognosis Web site[47]), allowing prediction of prognosis depending on geriatric parameters at the individual level, but they have not yet been studied specifically within the oncology population. Prognostic indices specifically focusing on older patients with cancer are needed; however, the ideal specificity of these instruments remains unclear. A validated GA for every disease and situation seems impossible to achieve. Because the cancer prognosis competes with other (age-related) causes of death, distinction between deaths resulting from cancer and other causes should be established whenever possible.[48]

Interpretation of key evidence. There is clear evidence that GA items independently predict OS in a variety of oncology diseases and treatment settings (level 4). Poorer OS in older patients with cancer and deficits identified in geriatric domains might potentially be explained by several factors (eg, increased risk of death resulting from causes other than cancer, increased death resulting from cancer because of less aggressive treatment, or death resulting from complications of cancer treatment). Therefore, disease-specific survival and OS should both be reported in trials of older patients with cancer (level 4). Several prognostic models for OS in the general geriatric population are available; however, these have not been specifically validated in older patients with cancer. Prognostic models for geriatric oncology are needed, including both cancer- and geriatric-related prognostic factors (level 4).

Question 5

What is the impact of GA findings on oncology treatment decisions?

Key evidence. We identified six new studies[15,16,23,27,39,49] conducted after 2010 that examined how GA results can affect oncology treatment decisions (Appendix Table A6, online only). The impact of GA on altering treatment choice varied significantly between the different available studies, ranging from 0% to 83.0%. The GA results more commonly led to a decrease in the aggressiveness of treatments, especially with regard to systemic therapies. It might sometimes be difficult to distinguish the effect of clinical impression (without GA) versus the independent effect of GA on treatment decision. One study[27] compared a treatment recommendation before GA was performed versus treatment recommendations after knowledge of GA results and found that GA did influence oncology treatment decisions (ie, lowering amount of prescribed drugs, reducing chemotherapy

intensity, or initiating supportive care) in 44.9% of patients. Decoster et al[49] found that patient age and clinical impression of the physician altered treatment choice in 45% of patient cases, whereas the addition of information provided by GA further changed treatment choice in only 5.0%, including both a decreased intensity of therapy (omission of treatment or dose reduction) as well as an increased intensity of therapy (standard therapy instead of dose reduction). GA also allowed pretreatment patient optimization, when remediable problems were unmasked.[23]

Interpretation of key evidence. Age by itself and clinical impression lead to treatment changes in a significant proportion of older patients with cancer, although the appropriateness of this judgment is underdocumented (it might lead to overtreatment or, more frequently, undertreatment)[3,4] (level 4). GA can additionally influence treatment decisions in older patients with cancer, either by decreasing or increasing treatment intensity (level 4). GA can inform key parts of the decision-making process to tailor treatment and trigger targeted GA-driven interventions (level 4). Oncology teams should integrate GA findings into treatment decisions (level 4).

Question 6

What should a GA comprise, including domains and tools?

Key evidence. Important domains in a GA are functional status, comorbidity, cognition, mental health status, nutrition, social status and support, fatigue, and assessment for polypharmacy and presence of geriatric syndromes, and various tools are available for assessing these domains. An overview of the different tools that were used in retrieved articles to assess the different domains of a GA in older patients with cancer is provided in Table 1. Classical oncology tools of functional status assessment like Eastern Cooperative Oncology Group or Karnofsky performance status have been shown to poorly reflect functional impairment in older patients with cancer.[50,51] Nearly all geriatric tools were developed in the general geriatric population and are subsequently being used in the geriatric oncology population. Tools describing polypharmacy and potentially inappropriate medications in older adults (eg, Beers criteria[35] and STOPP [Screening Tool of Older Person's Prescriptions] and START [Screening Tool to Alert Doctors to Right Treatment] criteria[36]) and sarcopenia[37] as a geriatric syndrome were added to the list of domains and tools because of their high relevance in geriatric care. Assessment of spirituality and religion is also relevant to both geriatric and oncology care.[52]

Most oncology teams and research groups use fixed combinations of tools in the original or adapted form; most of these are first- (eg, collection of single-domain, individually validated instruments) and second-generation instruments (eg, GA-introduced, health setting–specific comprehensive assessments).[53] Examples are the European Organisation for Research and Treatment of Cancer minimal data set[54]; Multidimensional Prognostic Index[55]; short, primarily self-administered GA tool developed by the Cancer and Leukemia Group B (Alliance)[19]; Mini Geriatric Assessment[56]; and National Comprehensive Cancer Network Senior Adult Oncology Guidelines,[57] which summarize various tools for assessing older patients with cancer. The online InterRAI-tool[58] is a standardized and internationally validated tool for assessing geriatric patients with different levels of clinical complexity across all health care settings (eg, home care, nursing homes, and acute hospitals). However, this more comprehensive tool is time consuming and has not been validated in oncologicy patients. The InterRAI Consortium[59] is in the process of developing a tool specifically for older patients with cancer.

Interpretation of key evidence. Important domains in GA are functional status, fatigue, comorbidity, cognition, mental health status, social support, nutrition, and geriatric syndromes (eg, dementia, delirium, falls, incontinence, osteoporosis or spontaneous fractures, neglect or abuse, failure to thrive, constipation, polypharmacy, pressure ulcers, and sarcopenia)[19] (level 5). Various tools are available to investigate these domains, and the superiority of one tool over another has not been proven. Choice of instrument might rely on local preference, aim of the tool, or resources present (level 5).

Question 7

How should GA be organized and implemented in clinical care?

Key evidence. Table 2 describes major models for implementation of GA in general geriatric medicine and in geriatric oncology, as well as the potential advantages and disadvantages of each approach. Three major models were identified. The first model is the creation of geriatric oncology units[60,66] within selected general oncology hospitals. This has the major advantage that geriatric expertise is centralized; however, the disadvantage is that this model can only reach a limited number of patients who are willing and able to travel to the geriatric oncology unit for consultation. Another model is to bring geriatric consultation teams[15,67] to patients who remain under the supervision of their treating oncologists. This model is possible in settings where oncology clinics are located within general hospitals with physician and multidisciplinary geriatric expertise. There is synergy in the care of this patient population, and therefore, this model has the potential advantage of reaching a large proportion of older patients with cancer. The crosstalk between oncology and geriatric teams allows for cross-fertilization of oncology and geriatric principles. Selected patients can also be referred to appropriate specific geriatric programs, such as a geriatric day care center, fall clinic, or memory clinic. The third model occurs in settings where geriatric expertise is not nearby (eg, stand-alone cancer centers without geriatric department or private practice oncology clinics). In these settings, GA can be performed to identify high-risk patients who could be referred to geriatricians outside of the cancer center (consultation or even electronic consulting[68]) or to members of a multidisciplinary team within the cancer center. Some comprehensive cancer centers have created nurse practitioner–led clinics to increase accessibility of care in regions with long distances to specialist care and/or long waiting lists resulting from a lack of geriatric staff in general hospitals.[69] Additional research is needed regarding the effectiveness of these models among patients with cancer.

Interpretation of key evidence. There are several ways of implementing GA in geriatric oncology (level 4). All models have advantages and disadvantages (Table 2), and preference should be given to models that fit with the local health care structure and setting. An assessment of outcomes should be built into the model and reported (level 5). Interaction with multidisciplinary geriatric teams (for selected patients) is highly recommended (level 5).

DISCUSSION

This article summarizes the review and interpretation of key evidence related to GA in geriatric oncology by the SIOG GA task force. We performed quality assessment of included studies. Because no randomized studies were available, and because of inconsistencies among

Table 2. GA Models in General Geriatric Medicine and Geriatric Oncology

CGA Model	General Geriatrics: Definition	General Geriatrics: Effectiveness
GA ward	Specific ward with specialized geriatric care team that applies GA and:	Six meta-analyses show that GEMU is most effective way of caring for geriatric patients with lower mortality, less institutionalization, and less functional decline compared with standard (non-GEMU) care for same patients[7,9,11,61-63]
GEMU	Delivers both acute and rehabilitative care to inpatients[11]	
ACE	Only delivers ACE; patients in ACE are transferred to long-term care facilities for rehabilitation programs[60]	
GCT	Specialized geriatric team that applies GA in non-GA wards on consultative basis	Recent meta-analysis[64] could not show consistent effect of IGCT interventions in non-GEMUs on mortality, readmission, length of stay, or functional status; absence of effect is mainly because of low adherence rate to IGCT recommendations
CMM	Joint geriatric and specialized care (eg, orthogeriatric beds or units)	Individual studies of CMMs, mainly operationalized as orthogeriatric beds to date, show promising results and advantages[65]

GA Model	Geriatric Oncology: Definition	Geriatric Oncology: Advantage	Geriatric Oncology: Disadvantage
Geriatric oncology unit	Specific ward with team specialized in caring for older patients with cancer that applies GA based on GEMU or ACE model[60,66]	Centralization of geriatric expertise and treatment options	Potential patient withdrawal from familiar treating oncologist; financial incentives might drive general oncologists not to refer patients; only limited No. of patients can be reached; general geriatric oncologists might miss detailed, rapidly evolving knowledge of broad field of oncology
GCT	Specialized geriatric team that applies GA in non-GA wards or in other settings on consultative basis[15,67]	Patients remain under supervision of their treating oncologists; can reach large majority of older patients with cancer; interaction between oncologists and geriatric teams is feasible	Decentralization of geriatric expertise has logistic and practical (eg, staffing) challenges; several factors may lead to low compliance of treating physicians to GCT advice; GA results may be unknown at time of treatment decision making; treating physicians might not know what to do with GA results; onset of geriatric intervention or treatment adjustment depends on local possibilities; patients who need referral to specific geriatric care programs might encounter waiting lists
Geriatric expertise not nearby	GA in standalone comprehensive cancer centers without geriatric department or private practice oncology clinic	Patients remain under supervision of their treating oncologists; validated methods can easily be used to target high-risk patients and introduce geriatric care; large majority of older patients with cancer can be reached	Realization of interaction between oncologists and geriatric teams is difficult; no gold standard to screen high-risk patients; inter-rater reliability and interpretation of results can be problem; patients who need referral might encounter waiting lists

Abbreviations: ACE, acute care for elders; CGA, comprehensive geriatric assessment; CMM, comanagement model; GA, geriatric assessment; GCT, geriatric consultation team; GEMU, geriatric evaluation and management unit; IGCT, inpatient geriatric consultation team.

some study results, the levels of evidence supporting the recommendations from this expert consensus panel were generally low.

Nevertheless, abundant information is present demonstrating that GA detects general health care problems in older patients with cancer that routinely are under-recognized in clinical oncology care. However, prevalence rates of geriatric conditions in any population correlate positively with the number of conditions evaluated for and strongly depend on selected tools, cutoffs for defining impairment, and the time points of evaluation.[70] There is general agreement regarding the domains of a GA; however, there are several different tools used to evaluate these domains, making cross-study comparison difficult. Therefore, future research should focus on standardization of assessment tools. Furthermore, there is a need to standardize interventions usng expertise from a multidisciplinary geriatric and oncology team. Performance capacity of various GA tools and the efficacy of interventions in different settings should also be considered. GA results should be documented in patients' medical records so that these results are available when treatment decisions are being made. This will require the development of algorithms for scoring and interpretation of the results for treating physicians. Future research should explore how problems detected by the GA and subsequent interventions interact with cancer care. Specifically, research is needed regarding the optimal way to communicate the information to the clinical team and how referrals for the implementation of GA-guided interventions should be organized.

GA has been shown to predict the risk of treatment-related complications (eg, chemotherapy toxicity or surgical risk), but toxicity prediction at the individual level remains moderate. This is likely because individual treatment toxicity is dependent on a variety of factors, including general host factors (eg, age, genetic predisposition, and capacity for metabolizing drugs), factors identified in a GA (eg, functional status, comorbidity, and others described in our article), treatment-related aspects (eg, choice of

therapy, including different regimens and drug-drug interactions), and tumor characteristics (ie, tumor aggressiveness affecting host). Although no causal relations could be determined, several general risk factors for treatment toxicity in older patients with cancer have been described. Further research should investigate if there are additional or specific risk factors among patients with specific diseases receiving specific treatment types. This should be investigated broadly for systemic therapies in addition to surgery, radiotherapy, or combined treatment modalities, leading to concise risk assessment models that can be implemented in everyday clinical practice. Similar trial design should be promoted, allowing cross-trial comparison in different settings. Biologic phenomena like genetic predisposition, drug metabolism, and drug-drug interactions can also have a major impact on the toxicity of specific drugs. Models should be built integrating both biologic and clinical aspects as well as geriatric parameters, which might predict toxicity better than each of these alone. Studies have generally focused on severe toxicity, mostly defined as grade 3 to 5. It should be recognized that specific grade 2 toxicities can also be associated with significant morbidity in older patients with cancer, and these drug-specific adverse effects should also be captured in study designs.[71]

The prognostic capacity for survival of existing GA-based models such as Eprognosis[47] should be explored in older cancer populations. Given the major impact of cancer-specific characteristics like tumor type, stage, and treatment, it is preferable to study this in uniform cancer populations where oncologic differences are small. The emerging big data systems combining patient and treatment information from electronic medical records present a unique opportunity for generating these data that should be harnessed. OS and treatment efficacy can also be significantly influenced by tumor biology, independent of the ageing process. For instance, similar tumors treated with identical therapy might respond differently because of differences in drug sensitivity. Personalized medicine for the tumor attempts to find the right drug and treatment for the right tumor, but personalized medicine should also titrate treatment to the host capacity to tolerate treatment. Future models should integrate biologic and GA aspects to further optimize the prognostic models.

Randomized trials comparing GA-guided therapy versus no GA are generally lacking in the oncology field. A fundamental question is whether level I evidence is required for incorporating GA in treatment decision making for older patients with cancer. Is it acceptable to omit GA in clinical trials, knowing that identified problems and subsequent interventions can influence important outcomes independent of treatment, as shown in the geriatric (nononcologic) literature? The effects of GA by itself are limited, unless followed by geriatric interventions, follow-up GA, and adaptation of care planning.[61] Measurement of blood pressure, weight, and blood count have also never been proven in randomized trials to be beneficial, but they are generally considered standard parameters essential for the basic evaluation of patients. Conversely, the geriatric world has been able to perform randomized GA trials and showed outcome benefit, so all efforts in this domain are encouraged.[7,9,11,61-63,71a]

Because local health care structures and settings can differ, various models for the implementation of GA in geriatric oncology are necessary. Governments should stimulate national or international implementation projects precluding every center from developing its own model. The use of uniform assessment is advised and encouraged, because it would allow benchmarking of patient or hospital data and would also allow transfer of the assessment results to other health care settings, such as primary and residential care. This has the potential for improving continuity of care and creating a uniform language for geriatric care problems and syndromes.[72] Further research also needs to focus on cost effectiveness of GA-directed intervention models in older patients with cancer with regard to key outcomes such as decreasing treatment toxicity, hospitalization, and readmissions.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Although all authors completed the disclosure declaration, the following author(s) and/or an author's immediate family member(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.
Employment or Leadership Position: None **Consultant or Advisory Role:** Hurria Arti, GTx (C), Seattle Genetics (C) **Stock Ownership:** None **Honoraria:** None **Research Funding:** Hurria Arti, Abraxis BioScience, GlaxoSmithKline **Expert Testimony:** None **Patents, Royalties, and Licenses:** None **Other Remuneration:** None

AUTHOR CONTRIBUTIONS

Conception and design: All authors
Financial support: Hans Wildiers
Administrative support: Hans Wildiers, Pieter Heeren, Cindy Kenis
Collection and assembly of data: Hans Wildiers, Pieter Heeren, Cindy Kenis, Arti Hurria
Data analysis and interpretation: Hans Wildiers, Pieter Heeren, Cindy Kenis, Koen Milisen, Arti Hurria
Manuscript writing: All authors
Final approval of manuscript: All authors

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Appendix

Methodology

Because geriatric assessment (GA) is a wide-ranging topic, the task force agreed for this recommendation article to select seven important and relevant questions upfront after input from all members. Unfortunately, other relevant topics (eg, prognostic capacity for maintenance of independence or quality of life) did not fall within the scope of this article.[71a]

A study was eligible for inclusion if it:

(1) Reported on older patients (mean or median age of study participants, ≥ 65 years) diagnosed with cancer (any type of cancer, including hematologic malignancies) and being seen in oncology clinics (outpatient oncology or hematology clinics or inpatient oncology or hematology units)
(2) Reported on cross-sectional, longitudinal, observational, or interventional studies focusing on GA and answering one of the seven questions on GA in geriatric oncology that we identified
(3) Was written in English, French, Dutch, or German
(4) Was published after November 16, 2010, and not included in systematic review by Puts et al[12] on GA

Excluded were editorials, case studies, reviews, expert opinion papers, and studies published as abstracts only. Studies investigating new drugs or treatment regimens were not included, because these addressed GA from another perspective and in preselected patient groups.

Data Sources

Our databank including PubMed, Embase, CINAHL, Medline (Ovid-SP), PsycInfo, and the Cochrane Library. Included articles were published between November 16, 2010, and March 7, 2013. We used keywords cancer and geriatric assessment.

Process From Study Selection to Final Draft

First study selection was based on titles and abstracts and performed by P.H. using the inclusion and exclusion criteria. In total, 1,204 titles and abstracts were reviewed. In case of indecision about the eligibility of a study, the article was considered as potentially relevant and proceeded to the full-text review stage. Nineteen studies remained after the full-text review stage.

A data abstraction form was predesigned by P.H. with Excel software. Abstracted information by P.H. included first author, year, study design, aim, location, sampling method, sample size, participant inclusion criteria, characteristics of included study participants, and results relevant to the seven questions.

Obscurities during full-text review by P.H. were discussed and clarified in consensus with H.W. The reference list of all selected studies was reviewed to obtain additional relevant articles. This added two articles. Retrieved articles were interpreted and discussed by experts, who could add relevant publications.

H.W., P.H., C.K., K.M., and A.H. established a first draft for each of the seven questions. Seven expert workgroups (for seven questions) were created to obtain concrete task force input. For all recommendations, data from the review by Puts et al,[12] as well as the newly selected publications, were used. Table 1 and Appendix Tables A2 to A6 summarize the recent publications, and we refer to the review by Puts et al[12] for the older data. After consensus within every workgroup was accomplished, a first integral draft was developed and sent to all task force members. Their suggestions were used to make new drafts until task group consensus was realized, with H.W. as the moderator. The Oxford 2011 levels of evidence[38] were used to grade the quality of evidence and strength of recommendations (Appendix Table A7).

Quality Assessment

The methodologic quality of included studies was separately evaluated by P.H. and C.K. using the methodologic index for nonrandomized studies.[14] We only performed a quality assessment on the studies that were initially retrieved by our literature search. Discrepancies between the scores were resolved by H.W. Results of quality assessment are listed in Appendix Table A1.

International Society of Geriatric Oncology Task Group on GA in Geriatric Oncology

Writing group. Hans Wildiers, Pieter Heeren, Cindy Kenis, Koen Milisen, and Arti Hurria.

Workgroup 1: What is the rationale for performing GA? Johan Flamaing, Riccardo Audisio, Lazzaro Repetto, and Eva Topinkova.

Workgroup 2: What information is provided by a GA beyond that captured in a standard history and physical exam? Theodora Karnakis and Martine Extermann.

Workgroup 3: What is the ability of GA to predict oncology treatment–related complications? Riccardo Audisio, Maryska L.G. Janssen-Heijnen, Supriya Mohile, Lazzaro Repetto, and Andrew Artz.

Workgroup 4: What is the association between GA findings and overall survival? Maryska L.G. Janssen-Heijnen, Claire Falandry, Barbara Van Leeuwen, Martine Extermann, and Etienne Brain.

Workgroup 5: What is the impact of GA findings on oncology treatment decisions? Supriya Mohile, Claire Falandry, Barbara Van Leeuwen, and Etienne Brain.

Workgroup 6: What should a GA comprise, including domains and tools? Martine Puts, Theodora Karnakis, Eva Topinkova, and Andrew Artz.

Workgroup 7: How should GA be organized and implemented in clinical care? Johan Flamaing and Martine Puts.

Table A1. Quality Assessment of Included Studies Using Methodologic Index for Nonrandomized Studies

Study	1 Clearly Stated Aim	2 Inclusion of Consecutive Patients	3 Prospective Collection of Data	4 End Points Appropriate to Aim of Study (+ ITT*)	5 Unbiased Assessment of Study End Points	6 Follow-Up Period Appropriate to Aim of Study	7 Loss to Follow-Up < 5%	8 Prospective Calculation of Study Size	9 Adequate Control Group	10 Contemporary Groups	11 Baseline Equivalence of Groups	12 Adequate Statistical Analysis	Total
Observational transversal													12
Aliamus et al[27]	2	2	NA	1	0	NA	2	0	NA	NA	NA	NA	7
Horgan et al[23]	2	1	NA	2	0	NA	0	0	NA	NA	NA	NA	5
Hurria et al[19]	2	1	2	2	0	NA	NA	1	NA	NA	NA	NA	8
Observational longitudinal													16
Kenis et al[15]	2	1	2	2	0	0	0	0	NA	NA	NA	NA	7
McCleary et al[21]	2	1	2	2	0	2	1	1	NA	NA	NA	NA	11
Aaldriks et al[34]	2	2	2	1	0	2	1	0	NA	NA	NA	NA	10
Soubeyran et al[33]	2	1	2	2	0	1	1	0	NA	NA	NA	NA	9
Klepin et al[32]	2	1	2	2	0	0	1	0	NA	NA	NA	NA	8
Hamaker et al[22]	1	2	2	1	0	2	1	0	NA	NA	NA	NA	9
Kanesvaran et al[26]	2	2	1	1	0	2	1	0	NA	NA	NA	NA	9
Hurria et al[20]	2	2	2	2	0	1	2	1	NA	NA	NA	NA	12
Clough-Gorr et al[18]	2	1	2	2	0	2	1	0	NA	NA	NA	NA	10
Caillet et al[16]	2	1	2	2	0	0	0	1	NA	NA	NA	NA	8
Shin et al[25]	2	2	2	1	0	2	1	0	NA	NA	NA	NA	10
Gironés et al[24]	2	2	2	1	0	2	0	0	NA	NA	NA	NA	9
Kristjansson et al[28]	2	1	2	2	0	2	1	0	NA	NA	NA	NA	10
Lazarovici et al[17]	2	2	1	1	0	0	0	0	NA	NA	NA	NA	6
Extermann et al[41]	1	1	2	2	0	2	1	1	NA	NA	NA	NA	10
Gironés et al[44]	1	2	2	1	0	2	1	0	NA	NA	NA	NA	9
Interventional													24
Spina et al[31]	2	2	2	1	0	2	1	0	0	0	0	0	10
Olivieri et al[30]	2	1	2	1	0	2	1	0	0	0	0	0	9

NOTE. Index is as follows: 0, not reported; 1, reported but inadequate; and 2, reported and adequate.
*Only considered in interventional studies.
Abbreviations: ITT, intention to treat; NA, not applicable.

Table A2. Reasons to Perform GA Based on Statements in Former Publications

Literature Search Results
GA can reveal/detect previously unknown and potentially reversible geriatric problems not found by routine oncology care[15,22,23,25,28,32-34,44]
GA can predict toxicity/adverse effects from cancer treatment or decrease in QOL, enabling more targeted use of preventive measures[15,18-21,23,25,32,41]
GA has important prognostic information that can be helpful in estimating life expectancy, which is of paramount importance when making treatment decisions[15,18,19,22-24,26,28-34,44,75]
GA can influence/improve treatment decisions[15,16,21,23,25,27,32]
GA allows targeted interventions, which can improve QOL and compliance with therapy[15,23,22,32]
GA is a systematic procedure to appraise objective health, including multimorbidity and functional status, which interfere with cancer prognosis and treatment choices in older patients[15,22,30]

Abbreviations: GA, geriatric assessment; QOL, quality of life.

Table A3. Problem Detection Through GA (global and per domain)*

Study	Year	Sample Size/Population	Age (years)	Patients in Whom GA Detected Problem (%)	GA Domain (%)							
					Demographic Data and Social Status	Functional Status	Presence of Fatigue	Presence of Comorbidities	Cognitive Problems	Depression	Nutritional Problems	Presence of Geriatric Syndromes†
Kenis et al[15]	2013	1,967 patients; six tumor types	Median, 76	NR 51.2‡	NR 10.2‡	37.7-56.5 30.5-40.1‡	69.4 36.6‡	— —	13.2 19.0‡	60.9 27.2‡	83.0 37.6‡	— —
Hurria et al[20]	2011	500 various patient cases of cancer	Mean, 73	NR	32.0-44.0	17.0-50.0	—	NR	NR	NR	34.0-60.0	Falls, 18.0; hearing, 25.0
Caillet et al[16]	2011	375 consecutive older patients with various cancers	Median, 79.6	NR	17.6	29.9-54.9	—	NR	27.1	28.3	57.5	Incontinence, 15.9; polypharmacy, 66.9
Soubeyran et al[33]	2012	348 patients; eight tumor types or cancers of unknown primary origin	Median, 77.45	NR	—	18.1-73.0	—	—	19.0	44.0	64.9	—
Hamaker et al[22]	2011	292 patients with known or first diagnosed cancers admitted to general medicine or oncology ward	Median, 74.9	91.1	43.8	26.0-76.9	—	—	15.1	65.3	46.0	Polypharmacy, 48.0; pain, 64.8; constipation, 22.1; incontinence, 25.2; decubitus, 1.4; delirium, 21.5
Kanesvaran et al[26]	2011	249 older patients with various cancers	Median, 77	NR	—	47.3-88.0	—	65.0	31.5-53.8	28.1	73.1	60.6
Gironés et al[24]	2012	83 patients with lung cancer	Median, 77	90. 4	NR	48.2-69.9	—	94.0-100.0§	26.4	31.3	44.6	Geriatric syndromes, 48.2; dementia, 26.4; falls, 22.9
Lazarovici et al[17]	2011	65 patients scheduled for colorectal cancer surgery	Median, 82.4	NR	NR	27.6-66.1	—	66.1	45.3	47.6		Incontinence, 20.0
Shin et al[25]	2012	64, newly diagnosed solid tumor except leukemia	Median, 71	NR	—	10.9-23.4	—	23.4	56.3	40.6	81.3	—
Aaldriks et al[34]	2013	55, advanced breast cancer	Mean, 76	NR	—	—	—	—	9.0-8.0	—	42.0	—
Klepin et al[32]	2011	54 patients with acute myelogenous leukemia	Mean, 70.8	92.6	—	40.7-53.7	—	46.3	31.5	38.9-53.7	—	—
Horgan et al[23]	2012	30 patients lung or GI cancer	Median, 78	NR 70.0‡	13.0 NR‡	20.0-53.0 NR‡	— —	60.0 60.0‡	NR NR‡	33.0 NR‡	37.0 NR‡	NR NR‡

Abbreviations: GA, geriatric assessment; NR, not reported.
*For studies published before November 16, 2010, see review by Puts et al.[12]
†Some studies have reported geriatric syndromes that overlap with other domains.
‡Data reporting on new detected problems (previously unknown to treating physician).
§Patients with at least one comorbidity.

Table A4. Predictive Value of GA (treatment complications)*

Study	Year	Trial Design	Type of Statistical Analysis Used	Multivariable Analysis Conducted? Adjustments Used?	Sample Size/No. of Events	Treatment Complications
Extermann et al[41]	2012	Prospective observational	Multivariable logistic regression model	Yes; forward-selection approach with predictors selected based on $P < .1$; adjustments for toxicity of regimen	518 patient cases of various cancers; 64% of patients experienced severe toxicity; 32% had grade 4 hematologic toxicity; 56% had grade 3 or 4 nonhematologic toxicity	In univariable analysis, diastolic blood pressure, IADL, aspartate aminotransferase, lymphocytes, and LDH were associated with grade 4 hematologic toxicity; ECOG PS, hemoglobin, creatinine clearance, albumin, MMS, self-rated health, and MNA were correlated with grade 3 to 4 nonhematologic toxicity; best performing model for hematologic toxicity included diastolic blood pressure, IADL, and LDH along with chemotoxicity (c-statistic, 0.76); best performing model for nonhematologic toxicity included ECOG PS, MMS, MNA, and chemotoxicity (c-statistic, 0.66); combination of two subscores (counting chemotoxicity only once) yielded model with c-statistic of 0.65; model established on first 331 patients and validated on subsequent 187 patients
Hurria et al[20]	2011	Prospective observational	Multivariable logistic regression model	Yes; variables with $P < .1$ in univariable analyses and clinically relevant variables (chemotherapy dosing [standard *v* dose reduced], No. of drugs [mono- *v* polychemotherapy], chemotherapy duration, and receipt of primary prophylaxis with WBC growth factor) examined in multivariable analysis	500 patient cases of various cancers; 53% of patients experienced ≥ one grade 3 to 5 toxicity (grade 3, 39%; grade 4, 12%; grade 5, 2%)	Predictors of severe chemotherapy complications: age (OR, 1.85; 95% CI, 1.22 to 2.82), cancer type (GI or GU; OR, 2.13; 95% CI, 1.39 to 3.24), chemotherapy dosing (OR, 2.13; 95% CI, 1.29 to 3.52), polychemotherapy (OR, 1.69; 95% CI, 1.08 to 2.65), hemoglobin (OR, 2.31; 95% CI, 1.15 to 4.64), creatinine clearence (OR, 2.46; 95% CI, 1.11 to 5.44), hearing (OR, 1.67; 95% CI, 1.04 to 2.69); falls (≥ one in past 6 months; OR, 2.47; 95% CI, 1.43 to 4.27), MOS (limited in walking one block; OR, 1.71; 95% CI, 1.02 to 2.86)
Aparicio et al[39]	2013	Prospective Randomized trial	Multivariable logistic regression model	Yes; variables with $P < .20$ in univariable analysis were tested using multiple logistic regression analysis	123 patient cases of metastatic colorectal cancer; 71 patients (58%) had grade 3 to 4 toxicity	Significant predictive factors for grade 3 to 4 toxicity: irinotecan arm (OR, 5.03; 95% CI, 1.61 to 15.77; $P = .006$), impaired cognitive function (OR, 3.84; 95% CI, 1.24 to 11.84; $P = .019$), impaired autonomy (OR, 4.67; 95% CI, 1.42 to 15.32; $P = .011$)
Badgwell et al[40]	2013	Prospective observational	Multivariable logistic regression model	Yes; variables significant ($P < .05$) in univariable analysis were included in multivariable analysis	111 patients undergoing abdominal cancer surgery; grade 1 to 2, 3 to 4, and 5 complications occurred within 90 days of surgery in 36%, 18%, and 3% of patients, respectively; because some patients experienced multiple complications, overall 90-day morbidity rate was 48% (n = 53)	No variables associated with morbidity
Shin et al[25]	2012	Prospective observational	Multivariable logistic regression model	Yes; variables with $P < .30$ in univariable analysis were tested using multiple logistic regression analysis; analyses adjusted by age, primary tumor type, treatment intent, relative dose-intensity, and MAX-2 index; association between significant toxicity and change in each GA parameter analyzed by repeated-measure analysis of covariance	64 patient cases of various cancers; significant toxicity noted in 16 patients (25.0%): 27.4% (three of 11 patients) in curative setting and 24.5% (13 of 53 patients) in palliative setting	ECOG PS ≥ 2 was only independent predictive factor for chemotherapy toxicity (OR, 38.52; 95% CI, 1.25 to 1191.97; $P = .037$); risk of significant toxicity was not significantly different according to frailty category; postchemotherapy changes in GA parameters were not associated with occurrence of significant toxicity
Falandry et al[42]	2013	Observational trial	Multivariable logistic regression model	Yes; covariates significantly associated in univariable analysis ($P < .1$) were included in multivariable analyses	60 older patients with metastatic breast cancer; No. of hematologic and nonhematologic toxicities was 60 and 59, respectively; No. of grade 3 and 4 toxicities was 65 and 13, respectively	Considering death, unplanned hospital admissions, and grade 3 to 4 toxicities, risk factors significantly associated by univariable and multivariable analyses were creatinine clearance ≤ 50 mL/min and living in nursing homes (no empiric data); only age ≥ 80 years (OR, 3.32; 95% CI, 0.99 to 11.20; $P = .022$) was related to nonhematologic grade 3 to 4 events

Abbreviations: ECOG, European Cooperative Oncology Group; GA, geriatric assessment; IADL, instrumental activity of daily living; LDH, lactate dehydrogenase; MMS, Mini Mental Health Status; MNA, Mini Nutritional Assessment; MOS, Medical Outcome Study; OR, odds ratio; PS, performance status.

*For studies published before November 16, 2010, see review by Puts et al.[12]

Table A5. Prognostic Value of GA*

Study	Year	Type of Statistical Analysis Used	Multivariable Analysis Conducted? Adjustments Used?	Sample Size/No. of Events	Age (years)	Mortality
Prospective						
Clough-Gorr et al[18]	2012	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; adjusted models validated using stepwise and backward regression analyses; adjustments made for age, stage, and education and marital status (fully adjusted)	660 patient cases of stage I to IIIa breast cancer only; events NR	≥ 65	All-cause and breast cancer–specific death rate at 5 and 10 years was consistently approximately 2× higher in women with ≥ three GA deficits (all cause, fully adjusted: 5-year HR, 1.87; 95% CI, 1.36 to 2.57; 10-year HR, 1.74; 95% CI, 1.35 to 2.15; breast cancer, fully adjusted: 5-year HR, 1.95; 95% CI, 1.18 to 3.20; 10-year HR, 1.99; 95% CI, 1.21 to 3.28)
Soubeyran et al[33]	2012	Logistic regression	Yes; variables significant in univariable analysis at 5% level selected for inclusion in multivariable model; forward-ascending stepwise selection procedure used; model adjusted for treatment site	348 patient cases of various cancers; within 6 months, 56 patients (16.1%) had died	≥ 70	
Hamaker et al[22]	2011	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; factors with $P < .20$ in univariable analysis and with < 20% missing data were included in multivariable analysis; backward selection procedure applied, accepting $P < .05$	292 patient cases of various cancers; mortality rate was 64% at 12 months	≥ 65	No GA-related parameters retained, but metastatic disease (HR, 1.67; 95% CI, 1.23 to 2.29) and tumor-related reason for admission (HR, 1.57; 95% CI, 1.12 to 2.21) were independent predictors of mortality
Kristjansson et al[28]	2012	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; adjustments made for cancer stage and age	176 patients cases of CRC only; events NR	≥ 70	GA frailty (HR, 3.39; 95% CI, 1.82 to 6.29), age, and cancer stage were independent predictors of mortality
Falandry et al[44a]	2013	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; geriatric variables reaching $P < .2$ and considered clinically relevant were included in Cox model to identify optimal combined set of geriatric risk factors, termed geriatric vulnerability parameters; these were used to predict survival by calculating GVS	109 patients with advanced ovarian cancer; of 27 patients who discontinued early, eight died; at last follow-up, 75 patients (68%) had died; median OS was 17.4 months (95% CI, 13.3 to 21.4)	≥ 70	Among patients with GVS ≥ 3, HR for premature death was 2.94 (95% CI, 1.79 to 4.84; $P < .001$) in univariable analysis (median survival, 21.7 *v* 11.5 months) and 2.89 (95% CI, 1.74 to 4.78; $P < .001$) in multivariable analysis after adjustment for FIGO stage (stage IV: HR, 2.19; 95% CI, 1.34 to 3.58; $P = .002$)
Spina et al[31]	2012	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; variables significant in univariable analysis at 5% level selected for inclusion in multivariable model; additional adjustments were not conducted	100 patient cases of DLBCL only; 5-year OS rate was 60% (95% CI, 50% to 69%); at time of writing, 65% of fit patients, 34% of unfit patients, and 31% of frail patients were alive ($P = .006$), with 5-year OS rates of 76%, 53%, and 29% ($P = .001$), respectively	≥ 70	Geriatric group (unfit: HR, 1.96; 95% CI, 1.04 to 3.70; frail: HR, 2.55; 95% CI, 1.14 to 5.73) and IPI score (2 or 3: HR, 1.95; 95% CI, 1.04 to 3.66; 4 or 5: HR, 4.93; 95% CI, 1.55 to 15.64) were independent predictors of death
Olivieri et al[30]	2011	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; following parameters were evaluated: sex, age, stage, IPI score, and group allocation; rituximab use and comorbidities were not evaluated, because of collinearity with group; variables reaching statistical significance at 90% level ($P < .1$) on univariable analysis were included in regression model for multivariable analysis	91 patient cases of DLBCL only; median follow-up of 57 months (range, 6 to 78 months); 42 patients were alive (31 fit patients, seven with comorbidities, and four frail patients)	Median, 74.4	Univariable analysis revealed age > 70 years and treatment group allocation to be significant factors predicting OS, but on multivariable analysis, group allocation was only independent factor

(continued on following page)

Table A5. Prognostic Value of GA* (continued)

Study	Year	Type of Statistical Analysis Used	Multivariable Analysis Conducted? Adjustments Used?	Sample Size/No. of Events	Age (years)	Mortality
Gironés et al[24,44]	2011, 2012	Log-rank test, Wilcoxon test, Kaplan-Meier method	NA	83 patient cases of lung cancer only; 59 patients had died at time of final follow-up	≥ 70	Factors related to survival (univariable): ECOG PS ($P <$ .001), IADLs ($P <$ .001), weight loss (P = NR), delirium (P = NR), incontinence (P = NR), dementia (P = .02), and depression ($P <$ .001); frailty was related to survival, but this finding was not statistically significant (P = .07); neither CCI nor SCS was related to survival (log-rank P = .47 and .24, respectively); stage significantly associated with survival (log-rank $P <$ .001)
Falandry et al[42]	2013	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; covariates significantly ($P <$ .1) associated in univariable analysis (hypoalbuminemia, living in residential homes) were included in multivariable analyses	60 patients with hormone-resistant metastatic breast cancer; eight patients died during treatment	> 70	Factors related to survival (univariable): hypoalbuminemia ≤ 30 g/L (HR, 12.5; 95% CI, 1.4 to 112; P = .024) and living in residential homes (HR, 0.95; 95% CI, 1.59 to 9.8; $P <$ .004); latter was only significant predictor of premature death in multivariable analysis (no empiric data of multivariable analysis were published)
Aaldriks et al[34]	2013	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; adjustment for age and comorbidities	55 patient cases of advanced breast cancer only; 41 (75%) of 55 patients had died after mean follow-up of 16 months	≥ 70	Inferior MNA (HR, 3.05; 95% CI, 1.44 to 6.45; P = .004) and GFI scores (HR, 3.40; 95% CI, 1.62 to 7.10; P = .001) associated with increased HR for mortality
Retrospective						
Kanesvaran et al[26]	2011	Cox regression analysis	Yes; reduced model selection carried out using backward stepdown by applying stopping rule of Akaike's information criterion among those significant parameters by means of univariable analysis; additional adjustments not conducted	249 patient cases of various cancers; events NR	≥ 70	Age (OR, 1.04; 95% CI, 1.01 to 1.07), abnormal albumin level (OR, 1.97; 95% CI, 1.23 to 3.15), poor ECOG PS (≥ $v <$ 2: OR, 1.77; 95% CI, 1.15 to 2.72), abnormal GDS (OR, 1.81; 95% CI, 1.29 to 2.56), advanced-stage cancer (OR, 1.71; 95% CI, 0.98 to 2.95), or moderate (moderate v low risk: OR, 1.59; 95% CI, 1.02 to 2.50) or high malnutrition risk (high v low risk: OR, 1.84; 95% CI, 1.17 to 2.87) tended to have shorter survival

Abbreviations: CCI, Charlson comorbidity index; CRC, colorectal cancer; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Obstetricians and Gynecologists; GA, geriatric assessment; GFI, Groningen frailty indicator; GVS, geriatric vulnerability score; HR, hazard ratio; IADL, instrumental activity of daily living; IPI, International Prognostic Index; MNA, Mini Nutritional Assessment; NA, not applicable; NR, not reported; OR, odds ratio; OS, overall survival; PS, performance status; SCS, simplified comorbidity score.

*For studies published before November 16, 2010, see review by Puts et al.[12]

Table A6. Impact of GA on Cancer Treatment Decision Making or Prediction of Cancer Treatment Delivery*

Study	Year	Sample Size	Impact of GA
Kenis et al[15]	2013	1,967	GA led to geriatric intervention in 286 patients (25.7%); for 282 patients (25.3%), treating physician stated that GA results influenced treatment decision in some way; GA results did not always reach treating physician before treatment decision was made
Decoster et al[49]	2013	902	In 42.2% of patients, clinical assessment led to different treatment decision compared with younger patients without comorbidities; in 56% of patient cases, treating physician consulted GA results before final treatment decision; in these patients, treatment decision was influenced by clinical assessment in 44.2%; in 31 (6.1%) of 505 patients, GA further influenced treatment, mostly concerning chemotherapy or targeted therapy; in eight patients, GA influenced physician to choose more aggressive chemotherapy; these patients had breast cancer and were age 70 to 82 years
Caillet et al[16]	2011	375	After GA, initial cancer treatment plan was modified for 20.8% of patients (95% CI, 16.8 to 25.3), usually to decrease treatment intensity (63 [80.8%] of 78 patients); by univariable analysis, cancer treatment changes were associated with ECOG PS $\geq$ 2 (73.3% in group with changes *v* 41.1% in group without; $P < .001$), dependency for $\geq$ one ADL (59.0% *v* 24.2%; $P < .001$), malnutrition (81.8% *v* 51.2%; $P < .001$), cognitive impairment (38.5% *v* 24.9%; $P = .023$), depression (52.6% *v* 21.7%; $P < .001$), and greater No. of comorbidities (mean, 4.8; SD, 2.9 *v* mean, 4.0; SD, 2.6; $P < .02$); by multivariable analysis, factors independently associated with cancer treatment changes were lower ADL score (OR, 1.25 per 0.5-point decrease; 95% CI, 1.04 to 1.49; $P = .016$) and malnutrition (OR, 2.99; 95% CI, 1.36 to 6.58; $P = .007$)
Aparicio et al[39]	2013	123	Dose reduction analyzable in 122 patients; 41 patients (33%) had reduction in dose-intensity > 33% during first 4 months after starting treatment; in multivariable analysis, significant independent predictive factors for reduction in dose-intensity > 33% were irinotecan arm (OR, 3.32; 95% CI, 0.99 to 11.20; $P = .022$) and alkaline phosphatase > 2× ULN (OR, 3.32; 95% CI, 0.99 to 11.20; $P = .022$)
Aliamus et al[27]	2011	49	GA led to changes in 44.9% of initial treatment plans; only 16.7% of these modifications occurred in frail patients (Balducci classification), whereas 60% occurred in vulnerable patients; treatment of vulnerable patients was significantly more frequently changed compared with fit or frail patients (OR, 4.9; 95% CI, 1.3 to 18.6; $P = .02$); principal treatment modifications in vulnerable patients were: change of chemotherapy, one drug instead of two (27.3%), chemotherapy dose adaptation (13.6%), supportive care (13.6%), confirmation of standard treatment without modification (22.7%); by univariable analysis, cancer treatment changes in vulnerable patients were associated with lowered MMSE and IADLs; multivariable analysis indicated lowered MMSE score (< 26) as only independent predictor for treatment modification in vulnerable patients
Horgan et al[23]	2012	30	When treatment plan was decided before GA (n = 24), it altered final decision in only one patient (4%); for those for whom treatment plan was undecided (pending further investigation and patient decision), findings on GA affected final plan in five patients (83%); only 60% of recommendations made for management of additional problems identified were implemented

Abbreviations: ADL, activity of daily living; ECOG, Eastern Cooperative Oncology Group; GA, geriatric assessment; IADL, instrumental activity of daily living; MMSE, Mini Mental State Examination; OR, odds ratio; PS, performance status; SD, standard deviation; ULN, upper limit of normal.
*For studies published before November 16, 2010, see review by Puts et al.[12]

Table A7. Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1)*	Step 2 (Level 2)*	Step 3 (Level 3)*	Step 4 (Level 4)*	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances†	Local nonrandom sample†	Case series†	NA
Is this diagnostic or monitoring test accurate? (diagnosis)	Systematic review of cross-sectional studies with consistently applied reference standard and blinding	Individual cross-sectional studies with consistently applied reference standard and blinding	Nonconsecutive studies or studies without consistently applied reference standards†	Case-control studies or poor or nonindependent reference standard†	Mechanism-based reasoning
What will happen if we do not add therapy? (prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case series, case-control studies, or poor-quality prognostic cohort studies†	NA
Does this intervention help? (treatment benefits)	Systematic review of randomized trials or n-of-one trials	Randomized trials or observational studies with dramatic effect	Nonrandomized controlled cohort/follow-up studies†	Case series, case-control studies, or historically controlled studies†	Mechanism-based reasoning
What are common harms? (treatment harms)	Systematic review of randomized trials, systematic review of nested case-control studies, n-of-one trials with patient about whom you are raising question, or observational studies with dramatic effect	Individual randomized trials or (exceptionally) observational studies with dramatic effect	Nonrandomized controlled cohort/follow-up studies (postmarketing surveillance) provided there are sufficient numbers to rule out common harm (for long-term harms, duration of follow-up must be sufficient)†	Case series, case-control studies, or historically controlled studies†	Mechanism-based reasoning
What are rare harms? (treatment harms)	Systematic review of randomized trials or n-of-one trials	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (screening)	Systematic review of randomized trials	Randomized trials	Nonrandomized controlled cohort/follow-up studies†	Case series, case-control studies, or historically controlled studies†	Mechanism-based reasoning

NOTE. Data adapted.[38]

Abbreviations: NA, not applicable; PICO, patients, intervention, comparator, outcomes.

*Level may be graded down on basis of study quality, imprecision, or indirectness (study PICO does not match question PICO); because of inconsistency between studies; or because absolute effect size is very small. Level may be graded up if there is large or very large effect size.

†Systematic review is generally better than individual study.