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Geriatric Oncology Research to Improve Clinical Care

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Summary

The incidence of cancer increases with advanced age. The Cancer and Aging Research Group (CARG), in partnership with the National Institute on Aging and National Cancer Institute, held a conference in September of 2010 which summarized the gaps in knowledge in geriatric oncology and recommendations to close these gaps. One recommendation was that the comprehensive geriatric assessment (CGA) should be incorporated within geriatric oncology research. The information from the CGA can be used to stratify patients into risk categories to better predict their tolerance of cancer treatment. CGA can also be used to follow functional consequences from treatment. Other recommendations were to design trials for older adults with study endpoints that address the needs of the older and/or vulnerable adult with cancer and to build better infrastructure to accommodate the needs of older adults to improve their representation in trials. In this review, we utilize a case-based approach to highlight gaps in knowledge regarding the care of older adults with cancer, discuss our current state of knowledge regarding best practice patterns, and identify opportunities for research in geriatric oncology. More evidence regarding the treatment of older patients with cancer is urgently needed given the rapid aging of the population.

Introduction

Cancer is a disease of aging; approximately 60% of all cancers and 70% of cancer mortality occur in persons aged 65 years and over.¹ The number of cancer patients over the age of 65 is projected to significantly increase over the next 20 years.² Aging is a highly individualized process, characterized by physiologic and psychosocial changes that can affect tumor biology, decision-making for cancer treatment, tolerance to treatment, and ultimately outcomes. Furthermore, there is heterogeneity in physiologic changes with aging. Historically, clinical trial enrollment of older adults has not reflected the more general population of older patients with cancer due primarily to: 1) the low overall numbers of older patients enrolled and 2) overly strict inclusion criteria leading to the enrollment of primarily healthy, “fit” older adults.³ It is very difficult to extrapolate clinical trial data to inform treatment decisions of older patients with cancer who are more vulnerable to adverse outcomes due to underlying health issues.⁴

Because the underlying health status of older persons included within clinical trials is not well-characterized, the results of studies evaluating the efficacy and tolerance of cancer treatment in older adults often conflict. Some authors suggest there is no significant relationship between the age of the patient and treatment decisions, delivered dose, toxicity,

or clearance rate of drugs, despite age-related physiologic changes.⁵ Others suggest consideration of several variables in the decision process, such as anticipated remaining life expectancy (RLE), the number and severity of comorbid conditions and a weighing of benefits versus risks of treatment using a comprehensive assessment of health status.⁶ Most authors agree that age alone should not be used as a rationale to deny chemotherapy to older patients.⁷

The evidence suggests that poor health status and functional limitations, comorbidity, cognitive decline, and/or limited social support correlate with toxicity to therapy and cancer outcomes.⁸ Although the commonly-used Karnofsky Performance Status (KPS) and Eastern Cooperative Oncology Group (ECOG) performance status (PS) measures do correlate with treatment toxicity, these tools alone do not reliably predict toxicity in the older adult.^{9–12} Comprehensive Geriatric Assessment (CGA), a compilation of standardized tools to assess geriatric domains such as comorbidity, functional status, nutrition, physical function, cognitive performance, and social support, can help define the “stage of the aging.”¹³ CGA can better quantify RLE, predict tolerance to treatment^{14–16} and add important information to the traditional PS assessment tools utilized in oncology.¹⁷ Unfortunately, clinical trial data that dictate evidence-based care for older patients with cancer have not generally included geriatric assessment tools.

The significant gaps in knowledge as related to cancer treatment in older and/or vulnerable adults led to the formation of the Cancer and Aging Research Group (CARG),¹⁸ a coalition of investigators dedicated to linking geriatric oncology researchers together to work towards a common goal of improving clinical care for older adults. CARG held a conference in collaboration with the National Institute of Aging (NIA) and the National Cancer Institute (NCI) entitled, “Clinical, Psychosocial, and Biological Correlates at the Interface of Aging and Cancer Research.”⁸ In this review, we utilize a case-based approach to highlight important knowledge gaps related to the clinical care of older adults with cancer, review recent progress and evidence from the literature that start to close the knowledge gaps, and indicate how one might begin to incorporate these practices into clinical care.

Assessment of Older Patients with Cancer: Moving Beyond Chronological Age

Case 1

SM is a 78 year old woman with hypertension, arthritis, and diabetes. She lives alone, but receives help from her daughter who lives nearby. She takes 6 medications and occasionally is forgetful in taking them. Her daughter assists her with taking her medications by maintaining her pillbox. She describes limitations in walking 1 block, primarily because of increased “joint aches” and she has fallen once in the last 6 months. She has been losing weight (15 lbs) which she attributes to a decrease in her social activities (her usual evening meal at the corner diner). On exam, her primary physician palpated a breast mass which was biopsied and revealed an infiltrating ductal carcinoma, which was “triple-negative” (ER(–), PR(–), HER-2/neu non-amplified). Blood work revealed her alkaline phosphatase was elevated, although other liver function tests are normal. Her creatinine is 1.3 mg/dL (creatinine clearance is 30 ml/min). Bone scan revealed findings suspicious of metastatic disease, which was confirmed at biopsy. Abdominal CT reveals metastatic disease to the liver. She presents today to discuss treatment options.

There are several reasons why it can be challenging to apply the results of cancer clinical trials into the treatment of older adults with cancer in the community. Several studies have demonstrated that the mean age of patients enrolled on cancer clinical trials is lower than the mean age of patients with the disease.^{19–21} There is considerable biological and

physiological heterogeneity and complexity in older adults, and this complexity is not typically addressed within our current clinical trials. Underlying health status assessment and geriatric domains are predictive of future morbidity and mortality in community-dwelling older adults, and they could affect cancer treatment tolerance and outcomes.^{9,16,22} These issues are very common in older cancer patients.^{23–25} In a large, nationally-representative database, it was found that functional problems and vulnerability due to adverse age-associated characteristics were more common in patients with cancer than in age-matched patients without cancer (Figure 1).²⁴ Underlying health issues and deficits in geriatric domains lead to significant heterogeneity in RLE for older adults, and an accurate estimation of RLE is important for making appropriate and relevant treatment decisions for cancer. Several studies have demonstrated that the older adults enrolled on clinical trials are at an increased risk for toxicity, suggesting that factors other than increased age may place many older adults at heightened risk for adverse outcomes.⁹

In order to bridge this knowledge gap, a more detailed assessment of the baseline characteristics of the older adults enrolled in clinical trials is needed. This would include evaluating (at least) the individual's functional status, comorbid medical conditions, psychological state, social support, nutritional status, and cognitive state. Collectively, this assessment is called a “comprehensive geriatric assessment” or CGA (Table 1).²⁶ Based on studies outside of cancer, each domain of a CGA is an independent predictor of morbidity and mortality in older adults.¹⁴ In addition to including these measures as part of the baseline evaluation, longitudinal inclusion of a CGA at standard timepoints would further our understanding of the impact of both the cancer and its treatment on these geriatric outcomes. The impact of therapy on function and cognition can be defining factors influencing the patient's preference for receiving treatment²⁷, as well as identifying the need for additional family support or community resources to assist the patient through the treatment course. While cancer clinical trial endpoints typically focus on disease-free and overall survival, additional endpoints may better guide the risks and benefits of therapy in an older adult, such as the impact of therapy on function and cognition. For example, the FOCUS-2 trial that evaluated chemotherapy for older and/or frail adults with colon cancer evaluated a composite endpoint of toxicity and perceived benefit by the patient in addition to standard response criteria,²⁸ providing meaningful information beyond the standard cancer endpoints to the clinician considering treatment in a frail older adult with colon cancer choosing.

Another routine part of clinical trials is to evaluate the toxicity of the cancer therapy as graded by the NCI Common Terminology Criteria for Adverse Events (CTCAE).²⁹ Grade 3 (severe or medically significant), 4 (life-threatening), or 5 (treatment-related mortality) toxicities are typically captured and reported in clinical trials and are considered to be “dose limiting.” However, several grade 2 toxicities may also be of importance to older adults with cancer. These toxicities are defined as moderate toxicities which may limit the patient's ability to complete instrumental activities of daily living, such as preparing meals or shopping for groceries. Age-associated changes in physiology may impact the ability of an older adult to withstand grade 1 or 2 toxicity. For example, grade 2 diarrhea (increase of 4–6 stools above baseline) might have significant consequences in an older adult, since aging is associated with an increased vulnerability to gastrointestinal side effects and fluid depletion.^{30,31} Grade 2 neuropathy may significantly affect performance status or increase the risk of falls in a vulnerable older patient. Furthermore, the longitudinal impact of lower grade toxicities is frequently not reported. This leads to an unanswered question of whether grade 3–5 toxicities are heralded by lower grade toxicities which could serve as a warning sign to modify the drug dosing.

Two recent studies rigorously evaluated the role of CGA for predicting toxicity from chemotherapy. Such predictive risk-stratification schemes allow clinicians to identify which patients are at highest risk for chemotherapy toxicity. In a study (n = 500) performed by CARG, CGA variables were associated with grade 3–5 toxicity.⁹ Risk factors for grade 3–5 toxicity included: 1) age ≥ 73, 2) cancer type (GI or GU), 3) standard dose, 4) poly-chemotherapy, 5) falls in last 6 months, 6) assistance with instrumental activities of daily living, and 7) decreased social activity. A risk stratification schema (number of risk factors: % incidence of grade 3–5 toxicity) which scored patients from 0–23 was developed. Over 80% of patients who scored 12 or more on the tool developed grade 3–5 toxicity. In contrast, the commonly used Karnofsky Performance Status scale was not able to identify which older adults were at increased risk. A second study, led by Dr. Martine Extermann, developed The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score in over 500 patients.³² The best model for hematologic toxicity included Instrumental Activity of Daily Living (IADL) score, LDH level, diastolic blood pressure, and chemotherapy intensity. The best predictive model for non-hematologic toxicity included performance status, Mini-Mental State score, Mini-Nutritional Score, and chemotherapy intensity. Information from two-thirds of the patients was used to develop the risk stratification scheme, and the tool was validated in the remaining one-third of patients.

As described above CGA variables can help identify older adults at increased risk of chemotherapy toxicity. In community-dwelling older adults, CGA can help estimate RLE and measures within CGA have been shown to influence survival in older patients with advanced cancer.^{33,34} Knowledge is growing on how CGA can be best incorporated within geriatric oncology research and for clinical decision-making. One conceptual model is that of “staging the aging” which would stratify an older patient's physiology capacity by underlying health status.¹³ Common terminology used include “fit” which represents the no significant CGA deficits versus “vulnerable” which captures mild CGA deficits and “frail” which captures significant CGA deficits such as severe comorbidity, activity of daily living deficit, or a clinically significant geriatric syndrome (e.g., dementia, falls).²⁴ Vulnerability and frailty represent patients who are along a continuum of increasing risk for morbidity and mortality. Incorporation of these tools and conceptual framework into clinical research, and potentially clinical care, can help identify which older patients are the most likely to tolerate and benefit from treatment. It can also help monitor aging-associated effects of treatment on outcomes that are especially important to older patients, such as function and cognition. These tools can be utilized in future research to identify and test interventions to reduce the development of chemotherapy toxicity in vulnerable older populations. Although not clinically applicable at this time, future research could also help gather biomarkers (e.g., inflammatory markers, telomere changes, genetic correlates of aging) that could help supplement the predictive value of clinical measures such as CGA.

Back to the case

SM has a recent diagnosis of metastatic breast cancer which is “triple negative”. Based on the CARG chemotherapy toxicity model for older adults,⁹ the following findings from the CGA identify SM's risk factors for chemotherapy toxicity: limitations in walking one block, physical health has decreased level of social activity, has a history of falls, and needs assistance with taking medications. Additional risk factors for chemotherapy toxicity include: decreased creatinine clearance and is greater than age 72. Based on these risk factors, this patient is at increased risk of chemotherapy toxicity (score of 12; >80% chance of grade 3–5 toxicity). Also, based on the CRASH score SM is at increased risk of hematologic toxicity due to chemotherapy based on need for assistance with instrumental activities of daily living. SM lives alone and has risk factors for falls and these issues should be addressed with interventions to boost caregiver/social support prior to initiation of

treatment. Several interventions could be considered including: utilizing chemotherapy that is hepatically metabolized (rather than renally metabolized since she has a decreased creatinine clearance), optimizing her social support, a nutritional consultation, consideration of Meals on Wheels, visiting nurse services to monitor her for toxicity, home safety evaluation with medical alert system for fall risk, and/or rehabilitation to improve functional status.

Improving Evidence-based Data on the Safety and Efficacy of Cancer Therapeutics in Older Patients

Case 2

MJ is a 75 year old man with coronary artery disease (status/post coronary artery bypass graft 2 years ago), hypertension, hyperlipidemia, and osteoarthritis. Medications include aspirin, atenolol, and lovastatin. Laboratory exam shows a mild microcytic anemia. Laboratories also reveal mild renal insufficiency with a creatinine of 1.2 and a glomerular filtration rate of 50. Carcinoembryonic antigen is normal. CT scans reveal a mass in the descending colon. The patient undergoes hemicolectomy. Pathologic exam reveals a stage IIIC (T3, N2) tumor. Geriatric assessment reveals that the patient requires assistance with IADLs, has frequent falls, and has a memory disorder. He is not very active and rests about 50% of the day.

The evidence for how to safely and effectively utilize cancer therapeutics for older and/or frail adults is limited. Although, for the most part, fit older adults do as well as their younger counterparts when receiving treatment within clinical trials, there is data suggesting that older adults are at increased risk for treatment-related toxicities.³⁵ Age-related physiologic changes may increase the risk of chemotherapy toxicity among older adults.⁹ Aging is associated with decreased intestinal absorption, changes in volume of distribution, decreased hepatic metabolism, and impaired renal excretion. Though studies do report differences in outcomes by age, the mechanisms behind these increased risks in toxicity is not well known. A common theme in recommendations from experts at the U13 conference was that factors that are known to be associated with an increased risk of toxicity (such as CGA variables and measures of organ [dys]function) should be routinely studied within clinical trials.^{9,36}

There remains a significant gap associated with age in the process by which data is gathered for cancer therapeutics in adults. The current oncology clinical trials structure often excludes patients with other medical problems or health conditions other than cancer, often excluding those with even mild organ dysfunction. There is also a common exclusion for patients with secondary cancers, even prevalent cancers such as prostate, breast, or colon treated definitively, that are in remission, and likely are cured at the time of trial participation. Both of these situations are much more common in older adults. Consequently, very few older patients have been included in FDA-registration trials. For example, only 9% of patients enrolled in registration trials were 75 years or older in FDA-registration trials.³⁷

Gaps in knowledge ultimately lead to wide variation in patterns of care in treatment initiation for older adults and increased health care costs.⁸ Bridging this gap requires attention on multiple levels. At the conceptual level, there should be closer attention to developing trials that are generalizable to the population as a whole. The proportion of older adults in trials should include those with underlying health status characteristics better reflecting the population of patients with the specific cancer and health statuses that are routinely seen in the community. At the development stage of research, a multidisciplinary team specifically including representation from geriatrics should evaluate whether or not the concept and protocol will meet these basic requirements. In addition, non-age-restricted clinical trials should strive to gather data including those from older cohorts. All trials,

especially trials studying therapeutics for cancers that occur commonly in older populations, should have a specific target accrual for patients aged 65 and over. Analysis of the safety and efficacy of the therapeutic agent related to age and health status should be undertaken. Progress could be facilitated if there was an FDA requirement for studies to include older adults in order to inform the geriatric usage section of the package inserts.

Although it may be possible to increase data in fit older adults by incorporating less strict exclusion criteria and by requiring a certain proportion of patients entered onto a trial to be older (especially for those cancers that are most common in older patients), it is more difficult to develop and conduct high-quality clinical trials for patients in the oldest age groups (e.g., >80 or over), and for those who are vulnerable or frail. For these patients, the important research questions may be different than for those who are younger and/or more fit. An older patient who is frail, who is treated with FOLFOX in the adjuvant setting, may discontinue therapy early due to toxicities and therefore not achieve a survival benefit. This same patient may be able to complete a therapeutic course of infusional 5-fluorouracil alone and achieve a greater benefit with a less intense regimen. It is often the case that new clinical trials test a standard approach against a more aggressive one. This research question is not always appropriate for the older, frailer individual where the efficacy and tolerability of the standard approach is highly questionable. The focus within oncology clinical research to always be “more aggressive” therefore continues to accentuate the current underrepresentation of older adults because the research study design focuses on pushing the envelope further (increased toxicity) rather than seeing if less toxic regimens can be equally efficacious. Unfortunately, funding for clinical trials in the United States for re-testing the appropriate dosing, efficacy, and toxicity of drugs already on the market in older patients is quite limited. Given the current incentives, without a mandate from leadership (NIH, cooperative group, or FDA) for this to change, it will be difficult to obtain the necessary data.

In vulnerable and frail older adults, the interactions between cancer, cancer treatment, and comorbidities impacts decision-making and survivorship. Specific studies of treatment algorithms are needed for patients who would otherwise be considered ineligible or unfit for most current treatment protocols. The CGA could be incorporated within eligibility criteria. For example, trials could be developed for patients who have functional deficits or a specific type, number, or severity of comorbidity. The geriatric oncology research community and researchers who attended the U3 conference series are actively trying to develop novel clinical trial study design to study therapeutics in older patients. Some of these designs would stratify patients by CGA at time of enrollment so that patients at different levels of health status receive more appropriate randomization options. Phase III trials that are not elderly-specific, but strive to enroll a generalizable proportion of older patients, should consider having the older patients complete CGA prior to randomization so that these factors can be used in the analysis of who is most likely to benefit. CGA has been shown to be feasible in this context within the cooperative group setting.³⁸ These issues will be addressed during the second U13 conference to be held in November, 2012. Trials that will lead to high impact data should be available for accrual at as many sites as possible -- including tertiary care institutions, cancer centers, and community settings. Supplemental incentives for enrolling patients onto these trials should be considered and trials should be available across different cooperative groups. In addition, high quality observational cohort studies that follow patients in the “real world” community setting with incorporation of CGA tools at defined time points could help bridge gaps in knowledge. An observational cohort study is a study that would prospectively follow a group of older cancer patients who have specific features in common over a defined period of time. Such studies examine predefined primary outcomes such as safety and efficacy of cancer treatments. Observational cohort studies are different than registries, which collect information on

incident events, but do not have prospectively defined outcomes, sample size, or duration of follow-up determined at inception. Rigorous observational cohort studies can complement randomized controlled trial data with information on efficacy, safety, and patient adherence with cancer treatment in a population of real-world patients.³⁹

Back to the case

The patient has several comorbidities including mild renal insufficiency. Geriatric assessment reveals he is frail due to underlying deficits and should be considered at high risk for toxicity from chemotherapy. His health status is poor. Unfortunately there is little data to guide the practitioner in weighing the risks and benefits of adjuvant chemotherapy for this patient. On the one hand, his cancer is high risk and has at least a 50% chance of recurrence. On the other hand, he has a high risk of toxicity from chemotherapy and possible adverse effects on function and cognition. At 75 years old in the lowest health status category, his life expectancy if he did not have cancer is estimated to be 5 years.⁴⁰ The best regimen to utilize for adjuvant treatment, FOLFOX or 5FU alone or capecitabine, is also controversial. A clinical trial that evaluated the risks and benefits of adjuvant chemotherapy in older, more vulnerable patients that measures not only survival but effects of treatment on function and cognition would help the practitioner and patient determine the best course of action. This case illustrates the significant gaps in knowledge that exist for older patients who are commonly seen in clinical practice and the need to further develop geriatric oncology research to gather evidence for these patients.

Improving Infrastructure for Older Adults with Cancer

Case 3

JO is a 75 y.o. African American man with diabetes (on insulin), hypertension, atrial fibrillation (on warfarin) and hearing loss presents with back pain. He is diagnosed with Gleason 7, metastatic prostate cancer. He walks with a cane, and had a fall without injury in the last year. His wife has Alzheimers' and he is the primary caregiver for her. They live in an apartment in an urban area, with a working daughter who visits on weekends, who does their shopping and helps organize their medications. He is started on androgen deprivation therapy injections every 3 months plus zoledronic acid infusions for osteoporosis. He misses the first scheduled follow-up appointment to start therapy, is 2 hours late to the next one, and he is considered "non-compliant" with therapy.

Another vital unmet need in geriatric oncology is the lack of clinical and research trial infrastructure that is compatible with the needs of most older adults. Specific barriers to trial treatment for older adults should be identified, and programs to overcome these barriers need to be developed if we are to optimally treat older adults. These barriers include (but are not limited to) difficulties with transportation to treatment centers, difficulty completing their daily activities, the frequent need to serve as a caregiver for an ill or dependent spouse, poor social support, and significant financial barriers, including the cost of medications or for paid caregiver time. Rarely do oncology clinic staffs have the necessary, specific training and time to handle geriatrics issues. When caring for older cancer patients in oncology offices, the necessary additional time is not usually provided to complete the consent process, perform relevant geriatric assessments, or to manage the higher likelihood of toxicities expected in this population. Furthermore, additional age-appropriate infrastructure to accomplish these tasks is rarely present to support participation in a trial, for frail, older adults. It will be difficult to improve trial enrollment without an upgrade in the infrastructure to support our most vulnerable of patients.

Given the above barriers, it is essential to build the necessary infrastructure to provide cancer care for older, frailer adults who compose the majority of cancer patients. This is

especially true for clinical trial enrollment, where older adults are less likely to be enrolled than their younger counterparts. Improvements in trial enrollment by older adults could potentially result from better tailoring oncology care to their unique needs. Examples would include wider, lower exam tables for patient comfort; easier access to necessary assistive devices such as wheelchairs; doorways and hallways to accommodate wheelchairs and to conduct geriatric assessment testing such as gait speed assessment. Additional time is typically needed to complete geriatric assessments, especially for the older, frailer patients. In addition, taking the treatments to the patients -- by developing and expanding community-based treatments and trials for older adults -- would eliminate the need for frail, older adults to travel long distances to participate in such trials. Research nurses and data managers should receive specific training in the care of older adults. Data collection from remote locations can also be improved by incorporating advanced technology. Home-monitoring programs using nurse or social-worker visits, telephone calls, or internet portals to support well-being during cancer therapy may be promising, and must be explored further.⁴¹

In addition, more consistent and earlier collaboration of oncologists with geriatrics is essential. A multidisciplinary team that includes providers with specific geriatrics training, should closely collaborate to design, implement, and execute specifically-designed clinical trials for older adults. Integrating geriatricians and other providers with specific geriatric training and experience into an older patient's treatment plan could reap great benefits. For example, it can improve adherence to therapies through careful attention to polypharmacy. It can help minimize the impact of toxicities, particularly if the patient has functional impairment or other comorbid conditions, by providing appropriate support throughout treatment regimens. Targeted assistance based upon particular comorbidities, such as cardiovascular disease or diabetes, is advised. The inclusion of other health care providers including clinical psychologists, social workers, physician extenders, and physical and occupational therapists, especially those with geriatrics training, is critical in treating older cancer patients.

The U13 grant and dissemination of the conference proceedings will hopefully help stimulate novel research ideas that will ultimately allow for the development of evidence-based recommendations to improve decision-making and outcomes of older patients with cancer. Although there is a wealth of information from geriatrics on how to improve outcomes in community-dwelling older adults, more research is needed regarding the impact of these evidence-based recommendations for geriatric oncology patients. A oncologist interested in practical recommendations on improving outcomes for older patients could refer to clinical guidelines and references.^{42,43}

Back to case

In treating this vulnerable older man with moderate grade prostate cancer, it is important to balance the need to control his cancer with androgen deprivation therapy with his advancing frailty - which is likely to be exacerbated by the therapy.⁴⁴ In addition, he has a number of social limitations that threaten his independence and prevent him from making it to clinic, including the need to care for his cognitively impaired spouse. Prior to starting on this therapy, every effort should be made to "prehabilitate" him with physical therapy in the home, provide additional social support to help maintain his independence, a home safety evaluation should be conducted to prevent more falls, and transportation to and from the hospital should be initiated. Given his fall history, he should be assessed for the need for an assist device, and a wheelchair should be provided during visits to the hospital. He and his family must be educated on the likely exacerbation of his diabetes with the initiation of androgen deprivation therapy, with careful monitoring of his blood sugars. And plans must be made for someone to care for his wife when he comes to appointments, as she is unable

to care for herself independently. His ability to be adherent with his therapy is more dependent on factors beyond his motivation, and he should not be labeled as “noncompliant”.

Conclusions

A multi-component and targeted approach, centered around CGA, that builds upon current infrastructure and incorporates new research priorities, is urgently needed to meet the needs of a rapidly aging population. Table 2 summarizes the most important gaps in knowledge and provides recommendations to help close the gaps in the next 10 years as identified by experts at the first U13 conference.³⁶ These mechanisms could help advance the research to close these gaps and improve care for older adults with cancer. Older patients, their families, and clinicians would ultimately benefit from research that improves the evidence base for oncology care in older adults. Focusing efforts in improving geriatric oncology research would ultimately help clinicians to provide higher quality of care to the most vulnerable of our patients with cancer.

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Figure 1.
Cancer is Associated with Functional Deficits, Vulnerability, and Frailty²⁴

Table 1Geriatric Domains, Related Research Questions, and Measurement Options.³⁶

Domains	Questions	Measurement Options
Function/Physical Performance	-Can baseline functional status and physical performance predict outcomes of older cancer patients? -How does cancer treatment impact functional status and physical performance?	Activities of Daily Living Instrumental Activities of Daily Living History of falls Timed Up and Go Short Physical Performance Battery Handgrip testing
Comorbidity/Pharmacy	-How do specific chronic diseases influence tolerance to cancer treatment? -How do we prevent adverse events in older patients with polypharmacy who are receiving cancer treatment?	Charlson Comorbidity Scale Cumulative Illness Scale-Geriatrics Comorbidity count and severity Medication Count Beers Criteria
Cognition	-How does underlying cognitive impairment affect cancer outcomes? -What is the impact of cancer treatment on cognition in patients with underlying cognitive impairment?	Mini-Mental Status Examination Blessed-Orientation-Memory Scale Short Portable Mental Status Questionnaire Montreal Cognitive Assessment
Psychological Status	-How does depression and anxiety affect cancer outcomes? -How does depression and anxiety affect adherence to treatment?	Geriatric Depression Scale Hospital Anxiety and Depression Scale
Nutrition	-Does weight loss correlate with functional decline in cancer patients?	Mini-Nutritional Assessment Weight loss Body Mass Index
Social Support	-How do we improve social support services to overcome barriers so that older patients can receive safe and effective treatment?	Needs assessment of financial capabilities, transportation, and caregiver status. Medical Outcomes Survey Social Support

Table 2Gaps in Knowledge and Recommendations to Close the Gaps³⁶

Gap 1: Clinical measures most relevant to older adults are rarely incorporated into oncology clinical trials	Geriatric assessment measures should be incorporated into trial design at baseline and subsequent endpoints.
Gap 2: Biological and Physiological Markers of Aging are Inconsistently Incorporated in Oncology Research	<p>There should be consistent incorporation of biological and physiological markers of aging in oncology clinical trials.</p> <p>--Study tumor samples to understand whether tumor biology changes with aging.</p> <p>--Study the relationships between inflammatory markers, aging, and cancer.</p> <p>-- Study the pharmacokinetics and pharmacodynamics of therapeutics in older patients.</p>
Gap 3: Too Few Studies Focus on Vulnerable Older Adults or Those Age 80+ Years	<p>There should be trials designed to answer clinical questions most applicable to older and/or frail adults.</p> <p>--Study alternative dosing strategies.</p> <p>--Include extra safety precautions.</p> <p>--Include quality of life and functional endpoints</p> <p>Observational cohort studies to capture data on patients not eligible for standard clinical trials should be considered.</p>
Gap 4: Clinical Trial Infrastructure Incompatible with Geriatric Needs	<p>Clinical trials should include infrastructure to accommodate age-associated conditions of older adults into research infrastructure.</p> <p>--Time for geriatric assessment</p> <p>--Exam rooms that accommodate older patients.</p> <p>--Offer resources to facilitate and support caregiving and transportation.</p> <p>--Provide geriatrics-specific training to research nurses and other support staff.</p> <p>--Allow for data collection from remote areas with technology to facilitate data collection.</p>