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Improving the Quality of Survivorship for Older Adults with Cancer

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Abstract

In May 2015, the Cancer and Aging Research Group (CARG), in collaboration with the National Cancer Institute and the National Institute on Aging through a U13 grant, convened a conference to identify research priorities to help design and implement intervention studies to improve the quality of life and survivorship of older, frailer adults with cancer. Conference attendees included researchers with multidisciplinary expertise and advocates. It was concluded that future intervention trials for older adults with cancer should: 1) rigorously test interventions to prevent decline or improve health status, especially interventions focused on optimizing physical performance, nutritional status, and cognition while undergoing cancer treatment; 2) utilize standardized care plans based on geriatric assessment findings to guide targeted interventions; and 3) incorporate the principles of geriatrics into survivorship care plans. Also highlighted was the need to integrate the expertise of interdisciplinary team members into geriatric oncology research, improve funding mechanisms to support geriatric oncology research, and disseminate high-impact results to the research and clinical community. In conjunction with the prior two U13 meetings, this conference provides the framework for future research to improve the evidence base for the clinical care of older adults with cancer.

Introduction

As the nation ages and expected survival from cancer lengthens, two-thirds of all cancer survivors will be aged 65 years and over by 2020.[1] Although older adults are disproportionately affected by cancer, high quality research focused on developing, evaluating and disseminating aging-specific interventions to improve the quality of survivorship of older patients with cancer is lacking.

In a recent Institute of Medicine (IOM) report, the existing geriatric oncology knowledge gaps were highlighted: “The current care delivery system is poorly prepared to address the care needs of this population, which are complex due to altered physiology, functional and cognitive impairment, multiple coexisting diseases, increased side effects from treatment, and greater need for social support.”[2] Under-representation of older patients in cancer

control and survivorship research has hindered progress in the development of aging-tailored interventions. There is a clear need for research on interventions to optimize the health of older cancer patients, especially those who have medical problems other than cancer or are in the "older-old" (70-80 years) and "oldest-old" (80+ years) subgroups.[3] Trials should be designed by interdisciplinary teams with expertise in aging and cancer to overcome the complex barriers and fundamental research design dilemmas in the study of cancer control and behavioral interventions for this population. In addition, improved models of care need to be implemented so that successful interventions can be delivered to older adults who represent the majority of individuals with cancer.

The need to significantly expand evidence-based research in geriatric oncology inspired the formation of the Cancer and Aging Research Group (CARG),[4] a coalition of researchers and advocates dedicated to improving the care of older adults with cancer. In 2010, CARG received U13 funding to conduct a series of three conferences on "Geriatric Oncology Research to Improve Clinical Care."[5-7] The third conference, "Design and Implementation of Intervention Studies to Maintain or Improve the Quality of Survivorship of Older and/or Frail Adults with Cancer" was held on May 13-14, 2015.

Methods

The conference goals were to "discuss knowledge gaps and methodological issues in the design and implementation of behavioral, cancer control, and survivorship intervention studies for older individuals with cancer." The conference addressed how to best design studies to improve outcomes of older patients who are receiving or have completed treatment for cancer. In addition, there were discussions on how to translate and disseminate what is known from clinical research in geriatrics and aging to improve care for older cancer patients.

The conference was limited to 70 leaders in cancer and aging research in order to promote active discussion. Participants included representatives from CARG, NIA, NCI, American Cancer Society (ACS), and Patient Centered Outcomes Research Institute (PCORI). Senior-level (n=45) and junior-level (n=19) investigators had interdisciplinary expertise in geriatrics, gerontology, oncology, psychology, nursing, exercise science, palliative medicine, nutrition, biostatistics, social work, and public policy. Also present were 6 patients and caregivers who are members of a PCORI-funded Advisory Board for a geriatric oncology clinical trial.

The content and speakers were selected by the U13 grant Co-PIs, Drs. Hurria, Dale, and Mohile, in collaboration with the oversight board. Speakers highlighted the current evidence that supports the design of interventions for older patients with cancer (Table 1). The presentations were transcribed and reviewed to identify research gaps and to highlight specific recommendations to "fill these gaps."

Moderated discussions followed the formal presentations to discuss mechanisms to close research gaps. Table 2 summarizes research recommendations for developing and

implementing intervention studies to improve the quality of life and survivorship of older individuals with cancer. The full conference is available on http://www.mycarg.org/home.

Gap 1: Geriatric Assessment Guided Interventions Are Needed to Improve Outcomes for Older Patients with Cancer

GA can be incorporated in oncology practice. As many as 50% of older patients with cancer screen positive for impairments in instrumental activities of daily living (IADL) and physical performance.[8, 9] Twenty percent are identified with cognitive disorders that would benefit from further work-up and management.[10] Older individuals with cancer have been found to have a higher prevalence of functional impairment, geriatric syndromes and frailty than older patients without cancer in population-based analyses.[11] Oncologists need a greater understanding of how to manage age-related health issues.

Measures within GA can identify patients at highest risk of chemotherapy toxicity or increased mortality (Table 1). GA factors not routinely captured in oncology clinical practice are independently associated with chemotherapy toxicity.[8, 12] In older patients with multiple myeloma (n>800), age, comorbidities, and cognitive and physical impairments identified patients who were most likely to have toxicity from therapy, discontinue therapy, and die.[13] Increasing data suggests that GA may help in estimating survival for older patients with cancer.[14]

In 2014, a Society of International Geriatric Oncology (SIOG) expert panel endorsed the use of GA in clinical practice for detection of impairment not captured by history or physical examination, for prediction of toxicity and survival, and for the ability to influence treatment decisions.[15] Despite growing evidence of its usefulness, GA has not been routinely incorporated into oncology clinical practice. Studies of care models utilizing GA to improve oncology-specific outcomes are underway.[16] Well-designed multi-component interventions to improve treatment decisions, toxicity, and overall survival of older adults with cancer are necessary.

Filling Gap 1: Re-designing Intervention Research for Older Cancer Patients

Future research should move beyond GA evaluation alone and focus on identifying biologic markers of frailty to improve the prediction of outcomes and to develop GA-guided interventions to improve outcomes. Biomarkers of chronic inflammation, cellular senescence, and sarcopenia may supplement or enhance GA measures to more precisely predict outcomes.[17] In older patients, frailty independently correlates with increased inflammatory markers and lower albumin levels.[18] While telomere length has had mixed associations with frailty and cancer prognosis, chemotherapy in older patients has been shown to increase levels of $p16^{INK4a}$ and studies are evaluating the role of this marker of senescence for predicting outcome (Table 1).[17] Sarcopenia has been associated with poorer survival in patients undergoing adjuvant chemotherapy for colon cancer,[19] with toxicities from targeted agents,[20] and with complications from surgery.[21] More research is needed to better understand the value of biologic markers for predicting outcomes.

GA information can influence decision making for cancer treatment.[22] Geriatricians utilize the GA to identify vulnerabilities in older adults and develop targeted interventions to

address impairments (i.e., care processes or management).[16] Examples include referrals to physical therapy for gait imbalance, counseling for nutritional deficiency, or initiation of treatment for patients with depression. GA can also guide alterations in the cancer treatment plan due to geriatric-specific issues; for example, selecting a less complex therapy option for patients with cognitive impairment.

In older adults without cancer, using GA to guide management has been shown in some studies to reduce mortality, decrease re-hospitalization and nursing home placement, and improve physical function.[23, 24] Hamaker and colleagues performed a systematic review of the effect of GA on management of older patients with cancer.[22] Seven studies suggest that the GA can be utilized to guide care management in this population. However, none of these studies evaluated cancer-specific outcomes. Two studies with geriatric oncology experts used the Delphi approach to inform how care processes could be created for each geriatric domain.[25, 26] A large study (n=1550) demonstrated that geriatric recommendations based on GA (e.g., referrals to dietician for nutritional impairment) were given to 76% of evaluable patients, but only 35% were implemented within oncology clinical practices.[27] Research is needed to understand the optimal delivery and implementation of GA evaluation and management programs. In addition, randomized controlled trials will be necessary to fully evaluate the potential benefits of these programs. Studies are underway (Table 1).

The recently published ESOGIA trial evaluated the role of CGA for guiding treatment for older patients with advanced lung cancer (Table 1).[28] In the standard arm, patients received doublet chemotherapy if they were <75 years and monotherapy if they were older or had a poor PS. In the intervention arm, CGA criteria were used to categorize patients into “fit” (doublet chemotherapy), “vulnerable” (monotherapy) or frail (best supportive care). Although survival endpoints were not different, patients in the intervention group had less overall toxicity and fewer treatment failures due to toxicity. Older patients who were fit received doublet chemotherapy more often than those in the standard arm. Those patients who were frail, almost a quarter of patients, were spared the toxicity of chemotherapy. Based on this, CARG considers the study results to be positive; CGA allowed for more appropriate treatment for those who will benefit and spared unnecessary toxicity among those who would not. In the future, randomized trials for older adults that incorporate CGA should include a true “usual care” arm where physicians are able to allocate treatments (rather than designated by age or PS). Future research should also evaluate the impact of implementing CGA-guided interventions on outcomes of older patients with cancer. Endpoints such as reducing toxicity and maintaining function should be weighted similarly to survival in importance.

Gap 2: Intervention Studies Should Focus on Meaningful Outcomes Appropriate for Older Patients with Cancer and Their Caregivers

Older patients may not wish to compromise quality of life or function (physical or cognitive) for survival benefits. In a pivotal study by Fried et al., 74.4% of older patients with a life-limiting illness would not choose treatment if it caused severe functional impairment and 88.8% would not choose treatment if it caused cognitive impairment.[29] Standard phase III trial end points do not capture key outcomes in geriatric medicine, including maintenance of

active life expectancy (i.e., the time an individual lives independently without significant disability) and preservation of function, cognition, and independence.[6] The inclusion of functional end points can aid in shared decision making by identifying the most important areas for intervention.

Toxicities from cancer-directed therapies including treatment related mortality are more common in older adults.[8] Because there is no regulatory requirement for establishing efficacy and toxicity of new therapies in older adults, lack of data in this population ultimately leads to expensive treatments being used in the non-clinical trial population (with more comorbidities) resulting in higher toxicity and smaller benefit. For example, population based studies of bevacizumab show that this drug is often given to patients with contraindications.[30]

The conference attendees discussed areas of need for geriatric oncology including comorbidity and polypharmacy, physical performance, nutrition, and cognition as well as attention to caregiver burden (Table 3). As patients become ill, caregivers become increasingly responsible for communication about age-related concerns with the health care team.[31] Caregivers of older patients may themselves require support due to their own health problems.[32] GA can help prioritize preferences, thereby allowing individualized support for each older patient and his/her caregivers.

Filling Gap 2: Develop Interventions for Older Patients with Cancer that Improve and Prevent the Progression of Age-associated Conditions

Interventions to improve or prevent decline in geriatric domains were determined by the group to be of high priority (Table 3). Studies should focus on older patients with cancer who have a high risk of adverse outcomes (due to underlying health status concerns or advanced disease) or those patients who will undergo treatments that are known to be highly morbid for older adults (e.g., abdominal surgery, chemotherapy/radiation, stem cell transplant). A “common” or “minimum data set” that incorporates both comorbidity and geriatric assessment tools could help foster comparisons across trials as well as be utilized for clinical decision making. Interventions should build upon the guiding principles for management of comorbidity as outlined by the American Geriatrics Society.[33] Research that evaluates physical performance and nutritional interventions should be tailored for patients in a way that would embrace the underlying complexity of health status. Given an increase in overlap between cancer and cognitive impairment, research priorities include how to best identify patients with cognitive impairment in oncology clinics, develop safe and effective cancer treatment plans for patients at high risk of worsening cognition, improve the understanding of overlapping biologic mechanisms of cancer and cognitive disorders, and develop research protocols for inclusion and protection of older patients with cognitive impairment. Research approaches can be adapted from other geriatric intervention protocols. For example, the effective Hospital Elder Life Program (HELP) which utilized non-pharmacologic interventions to prevent delirium in hospitalized patients could be adapted for older patients with cancer.[34] The impact of common supportive care medications for chemotherapy (e.g., benadryl, decadron) on instigating delirium should be investigated.

Outcomes should be chosen so that the interventions can be disseminated into routine supportive care if the study reveals positive benefits.

Novel trial designs that include adding geriatric assessment endpoints within an embedded study design or extending trials to ensure capture of a generalizable group of patients should be considered when studying interventions.[6] Composite endpoints which can integrate non-efficacy aspects of treatment may provide information that is more relevant to older adults. An example of a composite endpoint in older individuals is 'therapeutic success' which combines efficacy, toxicity and patient's adherence with treatment.[35] In one study, this was defined as a patient receiving a pre-defined course of chemotherapy and having a response without experiencing grade III/IV toxicity.[36] In the FOCUS-2 study, a positive "overall treatment utility" indicated absence of disease progression with no major negative treatment effects in terms of toxicity or patient acceptability.[37]

Alternatives to traditional study designs are needed to better answer clinically meaningful questions for the majority of older patients with cancer. The typical older adult with cancer has multiple comorbidities or cancer symptoms that make them ineligible for traditional randomized controlled clinical trials. In addition, the intervention needs to be implemented with high fidelity and low flexibility, which can limit the generalizability to general practice. In contrast, the pragmatic trial has fewer eligibility criteria, takes place in a routine clinical setting, and has high external validity.[38] The pragmatic trial design allows for heterogeneity in health status of older patients with cancer and flexibility related to implementation of the intervention. Another option is to evaluate the impact of interventions already studied in older patients without cancer in projects designed for quality improvement. This approach may be applicable for the study of fall and delirium prevention programs for older patients with cancer. Data generated from pragmatic trials and quality improvement projects are more generalizable to the "real-world" where patients are getting treated.

Gap 3: Cancer Survivorship Plans and Programs Should Better Address the Needs of Older Patients

Two thirds of all cancer survivors will be aged 65 or older by 2020.[1] Clinically important long-term effects of cancer in the older adult include fatigue, cognitive impairment, chemotherapy induced peripheral neuropathy, physical limitations, and osteoporosis.[39] Early recognition and management may prevent disability and chronic conditions.

Many groups have advocated for routine incorporation of survivorship care plans (SCPs) into clinical care.[39] SCPs include treatment summaries, surveillance plans, as well as lifestyle information tailored to the survivors of specific cancers, and are provided towards the end of active, usually curative intent, treatment. How SCPs can reduce the fragmented care that older patients with complex needs often encounter is an important area of future research in cancer care delivery.

Filling Gap 3: Focus More Studies on Survivorship Care for Older and/or Frail Adults with Cancer

Given that the majority of survivors are older, applying survivorship guidelines to the older adult should be considered the rule, not the exception. The U13 attendees recognized that

there is considerable need for more research to understand the advantages and disadvantages of SCPs since the format, timing, and outcomes are still uncertain. However, addressing the needs of older adults in the context of survivorship research, including access to patient-centered, non-fragmented care, was deemed to be high priority. The provision of SCPs to cancer survivors is infrequent. In the cooperative group setting, only 35% of 328 older women with invasive, non-metastatic breast cancer received SCPs and older age was associated with lack of receipt.[40] SCP receipt was associated with greater knowledge regarding breast cancer, but not improved function. To impact function, SCPs should include information tailored to the needs of older patients including exercise, nutrition, polypharmacy, social support, and comorbidities. In a study of over 1500 cancer survivors, Leach et al. found that on average, survivors reported 2 medical conditions diagnosed after cancer.[41] Body mass index, activity level, and time from diagnosis were associated with higher reported comorbidity.

The participants at the U13 meeting agreed that research priorities should include: evaluation of the best approaches for delivery of SCPs to older patients, investigation of how to best tailor SCPs for older patients by utilizing geriatric assessment to outline health concerns, evaluation of care coordination models that outline the responsibilities of various providers for comorbid conditions, and determining how to best partner with caregivers in the delivery of care. Research to close gaps in knowledge should include patients from different socioeconomic backgrounds, foster deliberate efforts to improve data collection tools, improve recruitment and retention, and focus on testing different models of care for survivorship care delivery.

Gap 4: Research for Older Cancer Patients Should Include Input from Interdisciplinary Teams with Aging Expertise

Interdisciplinary teams with aging expertise are central to providing optimal care to the older patient with cancer. In clinical disciplines, teams should include expertise from medicine, nursing, social work, physical therapy, occupational therapy, and nutrition. Depending on the clinical question, pharmacists, psychologists, counselors, chaplaincy, and professionals with cognitive expertise should also participate in team-based care. Interdisciplinary teams foster the coordination of care and can improve outcomes for patients with complex medical and psychosocial needs. For example, co-management of older patients undergoing surgery with geriatric trained advanced practice nurses and pharmacists was associated with a higher likelihood of discharge to the community.[42] Within a geriatric oncology clinic setting, a pharmacy intervention delivered recommendations to reduce medications and potential drug interactions were provided in 75% of patients.[43] Despite increased awareness of the benefits of interdisciplinary teams in the clinical care of older patients, the team-based approach does not often extend into the planning and implementation of geriatric oncology research.

As demonstrated through efforts by PCORI, incorporating patient and caregiver preferences and values into research planning is also important. In an era of scarce resources, partnerships between advocates and researchers to identify the highest research priorities, examine feasibility of study design and interventions, and determine the importance of endpoints are needed.

Filling Gap 4: Incorporate Input from Multiple Stakeholders into Geriatric Oncology Research

Integration of input from geriatrics disciplines should be a priority for every research study that includes older adults with cancer. As in clinical practice, interdisciplinary team training programs can improve knowledge and attitudes about aging, team skills, and interprofessional communication and collaboration. The NCI-ASCO initiative on team-based care delivery will help provide insight on how to best foster team science.

As discussed by the advocate stakeholders at the U13 meeting, older patients and caregivers can help humanize the science, bridge the researchers with the lay community, build public support, and help disseminate research findings in culturally appropriate ways. In one example, a 13-member older patient and caregiver advisory group to a PCORI-funded study has provided continuous input to inform study design, recruitment materials, consent forms, and other study documents.

Although older adults with cancer constitute the majority of patients seen in oncology clinics, the overall awareness of geriatric oncology issues among the general public and policymakers remains low. Traditionally, results are shared via journal articles and scientific conferences, but this approach has limited impact on wider practice and policy. Other options for public knowledge translation include dissemination and implementation (D&I) science and evidence-based storytelling. D&I research systematically examines factors influencing the integration of a new practice or treatment into routine care focused on outcomes most relevant for stakeholders.[44] Evidence-based storytelling, which provides narratives to illustrate policy issues, is likely to be effective for the general public and policymakers because it puts an individual patient's or clinician's story in a context that is understandable and compelling. A multi-prong dissemination approach may be more effective in moving geriatric oncology into the forefront of health care dialogue.

Summary

There is a dearth of research studies that contain measures and methods appropriate for building an evidence base reflecting the typical population of older adults with cancer. For older adults, age alone does not properly characterize physiological heterogeneity. This heterogeneity has profound implications for research team composition, study design and end point selection. Mortality is the outcome of choice for clinical trials, yet alternative outcomes such as functional independence may be more meaningful for older adults. The NIH, ACS, and PCORI have funding opportunities to support the development and implementation of interventions to improve quality of life and survivorship for older adults with cancer. Moving forward, investigators should utilize research approaches outlined in the U13 series of manuscripts[5-7] to help answer relevant questions regarding the risks and benefits of interventions for vulnerable adults with cancer.

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Table 1

Examples of Geriatric Oncology Research that Supports Behavioral, Cancer Control, and Survivorship Interventions

Research Priority	Study	N =	Age (y), Characteristics	Objective	Results
GA	Hurria, et al[8]	500	Median age 73; Mixed solid tumor types and lymphomas	To develop a predictive model for grade 3 to 5 toxicity	Grade 3 to 5 toxicity occurred in 53% of patients; Predictive factors included age ≥ 72, tumor type, chemotherapy dosing and number of agents, anemia, reduced creatinine clearance, hearing loss, history of falls, needing medication assistance, reduced ability to walk one block and decreased social activities due to health
GA	Extermann, et al[12]	518	Median age 76; Mixed solid tumor types and lymphomas	To create and validate a list of variables used to predict chemotherapy toxicity	Severe toxicity observed in 64% of patients; Predictors of hematologic toxicity were lymphocytes, AST level, IADL, LDH, DBP and chemotherapy intensity; Predictors of nonhematologic toxicity were hemoglobin, creatinine clearance, albumin, self-rated health, ECOG PS, MMSE, MNA and chemotherapy intensity.
GA	Karnesvaran, et al[14]	249	Median age 77; solid tumor malignancies included	To determine the impact of each GA domain on OS	Age, albumin, ECOG PS, GDS score, high malnutrition risk and advanced disease were independent predictors of survival.
GA	Palumbo, et al[13]	869	Median age 74, newly diagnosed MM patients	To identify a scoring system based on geriatric parameters to predict OS	Age, comorbidities, cognitive and physical impairments identified patients who were most likely to have toxicity from therapy, discontinue therapy, or die.
GA and management	Caillet, et al[45]	375	Mean age 79.6, solid tumor malignancies included	To identify GA components independently associated with changes in planned cancer treatments	After GA, initial treatment plan was modified in 20.8% of patients; factors independently associated with cancer treatment changes were ADL score and malnutrition.
GA and management	Kalsi, et al[46]	65	Mean age 75.8; all types of cancer	To evaluate the impact of geriatrician-delivered GA interventions on chemotherapy toxicity and tolerance	Participants received a mean of 6.2 interventions (range 0-15). They were more likely to complete cancer treatment as planned compared to a historical cohort.
GA and management	Baitar, et al[27]	1550	Patients age ≥70 at time of diagnosis of cancer or disease progression	To describe and evaluate the implementation of geriatric recommendations based on GA	A median of 2 geriatric recommendations (range 1-6) were given to 76% of the evaluable patients (n=710). 35% of all the recommendations were performed. Most common were referrals to dietician, social worker, and psychologist.
GA and management	Corre et al[28]	494	Patients age ≥70 with advanced lung cancer	To evaluate the impact of CGA allocated treatment on treatment failure free survival	Although there was no improvement in survival outcomes, the prevalence of overall toxicities (85.6% vs 93.4%, p=.015) and treatment failures as a result of toxicity were significantly decreased (4.8% vs 11.8%, p=.007) in the CGA arm.
Physical Activity and Nutrition	Morey, et al[47]	641	Survivors aged 65-91 years who were overweight	To evaluate the impact of a home-based telephone and education program on mediating functional decline in RCT	Mean functional scores on SF-36 declined less rapidly in the intervention group. Physical activity, dietary behaviors and QoL increased significantly in intervention group compared with control group. Weight loss was greater in the intervention group.

Research Priority	Study	N =	Age (y), Characteristics	Objective	Results
Survivorship	Faul, et al[40]	328	Women with invasive, nonmetastatic breast cancer	To examine the receipt of SCPs among older breast cancer survivors and association with outcomes	35% of women received SCP. Increasing age was associated with lower odds of receiving SCP. SCPs were associated with greater knowledge and understanding; however functioning was not significantly different.
Ongoing study: GA and management	Mohile, et al	688	Patients age ≥70 with advanced solid tumor malignancy receiving treatment	To compare GA with management to usual care for reducing chemotherapy toxicity	Study Ongoing
Ongoing study: Biologic Predictors of Outcome	Hurria, et al	500	Patients age ≥65 with stage I-III breast cancer receiving adjuvant chemotherapy	To identify clinical and biological predictors for toxicity to adjuvant and neoadjuvant chemotherapy in older breast cancer patients	Study Ongoing
Ongoing study: Physical Activity and Biomarkers	Muss, et al	100	Breast cancer patients age ≥65	To evaluate the impact of a physical activity intervention program on biomarkers of aging and body composition	Study Ongoing

GA = Geriatric assessment; PS = Performance status; ADL = Activities of Daily Living, IDL = Instrumental Activities of Daily Living; AST = Aspartate aminotransferase level; LDH = Lactate Dehydrogenase; DBP = Diastolic blood pressure; MMSE = Mini Mental Status; MNA = Mini Nutritional assessment; OS = overall survival; MM = Multiple myeloma; SCP = Survivorship Care Plan

Table 2

Research Recommendations for Developing Intervention Studies to Improve Quality of Life and Survivorship for Older Patients with Cancer

1	In studies of behavioral or cancer control interventions, the percentage of older adults enrolled in standard clinical trials should reflect the proportion of older patients in the general population.
2	Studies are needed to better understand on how cancer and its treatments interact with underlying vulnerabilities, which in turn impacts our understanding of the feasibility, safety, and efficacy of interventions for this population.
3	Extrapolating evidence on interventions for common problems (e.g., falls, cognitive impairment, delirium) impacting the health status of older adults with cancer would be beneficial from studies in older patients without cancer, but studies are still needed to determine how to tailor these interventions for older patients with cancer.
4	Studies should incorporate knowledge on trial design, infrastructure support, and methodology that is known from existing research focused on the aging population without cancer.
5	Partnership with stakeholders, including older patients, caregivers and interdisciplinary team members with geriatric expertise, should occur at the very beginning of research development.
6	Issues that should be considered during study development include how the intervention will bedelivered in the community and cost considerations.

Table 3

Research Gaps and Mechanisms to Close the Gaps *

Research Priority	Research Gaps	Mechanisms to Close the Gaps
Function	Which specific pre-treatment functional measures best predict toxicity to cancer treatment?	Capture measures of function prior to starting treatment
	How can we develop interventions to improve outcomes in patients with functional impairment?	Develop and test interventions (mobility, fall prevention, and exercise) tailored for older patients with cancer
	How do specific cancers and treatment regimens influence long-term functional outcomes?	Capture measures of function longitudinally after or during treatment
Comorbidity	How do specific comorbidities and their interactions influence cancer treatment toxicity, cancer outcomes, survivorship?	Capture changes in comorbidity over the course of treatment and in survivorship period
	How do we estimate life expectancy in older patients with cancer and comorbidities, with or without cancer treatment?	Develop and test measures of remaining life expectancy prospectively in patients with cancer and comorbidities who are and who are not receiving treatment
	How do we develop and successfully complete clinical trials for patients with comorbidities?	Consider alternate trials designs such as pragmatic and extended trial designs
Polypharmacy	How can we identify polypharmacy and measure risk of adverse events due to drug interactions, including chemotherapy, in older cancer patients?	Include older patients in early phase clinical trials and capture medication changes over the course of study in order to determine relationships with toxicity
	How do we tailor medication lists to best reduce risk in older patients receiving treatment for cancer?	Develop and test interventions incorporating pharmacists and that offer care coordination with primary care
Cognition	How should we assess cognition and decision-making capacity for oncology clinical trials?	Evaluate utility of cognitive measures for identifying patients at high risk for cancer treatment
	What are the side effects of cancer treatment in older patients with cognitive impairment?	Capture measures of cognition before initiation of treatment and follow outcomes in prospective, observational cohort studies
Psychological Status	How does depression/anxiety affect treatment choices and compliance in cancer patients?	Examine the impact of depression and anxiety in decision-making for treatment and medication compliance
	Are there interventions that could help patients and caregivers with depression/anxiety or fear of cancer recrurrence?	Develop and test multidisciplinary interventions to intervene on depression/anxiety and fear of recurrence in older patients with cancer and their caregivers
Nutritional Status	How does nutritional status and weight loss affect prognosis in older patients?	Examine the effects of nutritional status on outcomes, including efficacy and safety of cancer treatment, in older patients
	Are there supportive care interventions that could help mediate nutritional problems in older patients with cancer?	Develop and test nutritional interventions tailored for older patients with cancer
Social Support	How does the perceived quality of social support relate to treatment practice patterns in older adults with cancer?	Examine the perceived quality of social support as a predictor of treatment practice patterns and outcomes
	Can infrastructure be strengthened to address social support issues of older cancer patients and caregivers?	Test the efficacy of clinical teams (including social work, care managers, or navigators) for assisting older patients with cancer and their caregivers

* Updated from Dale et al. JNCI, 2011[5]