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Improving the Evidence Base for Treating Older Adults With Cancer: American Society of Clinical Oncology Statement

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ABSTRACT

The American Society of Clinical Oncology (ASCO) convened a subcommittee to develop recommendations on improving the evidence base for treating older adults with cancer in response to a critical need identified by the Institute of Medicine. Older adults experience the majority of cancer diagnoses and deaths and make up the majority of cancer survivors. Older adults are also the fastest growing segment of the US population. However, the evidence base for treating this population is sparse, because older adults are underrepresented in clinical trials, and trials designed specifically for older adults are rare. The result is that clinicians have less evidence on how to treat older adults, who represent the majority of patients with cancer. Clinicians and patients are forced to extrapolate from trials conducted in younger, healthier populations when developing treatment plans. This has created a dearth of knowledge regarding the risk of toxicity in the average older patient and about key end points of importance to older adults. ASCO makes five recommendations to improve evidence generation in this population: (1) Use clinical trials to improve the evidence base for treating older adults with cancer, (2) leverage research designs and infrastructure for generating evidence on older adults with cancer, (3) increase US Food and Drug Administration authority to incentivize and require research involving older adults with cancer, (4) increase clinicians' recruitment of older adults with cancer to clinical trials, and (5) use journal policies to improve researchers' reporting on the age distribution and health risk profiles of research participants.

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INTRODUCTION

The Institute of Medicine (IOM) report "Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis"[1] (hereinafter referred to as IOM quality report) highlights the need to improve the evidence base for treating older adults with cancer. Older adults experience the majority of cancer diagnoses and deaths and make up the majority of cancer survivors.[2-4] However, the evidence base for treating this population is sparse, because older adults are underrepresented in clinical trials, and trials designed specifically for older adults are rare.[5] The Cancer and Aging Research Group, in collaboration with the National Cancer Institute (NCI) and National Institute on Aging (NIA), received a U13 grant to conduct and disseminate a series of workshops on geriatric oncology research. However, there are few policy initiatives targeting the lack of evidence on older adults. In response to this problem, the American Society of Clinical Oncology (ASCO) convened a subcommittee of the Cancer Research Committee to develop an ASCO statement on improving the evidence base for treating older adults. ASCO presents a series of recommendations to improve evidence generation in this population.

PROBLEMS

The major drivers creating the need to generate more evidence on the treatment of older adults are: (1) the aging US population, (2) the underrepresentation of older adults in clinical research, and (3) the clinical implications of the lack of evidence in older adults on the quality of care.

Aging Population

The US population is aging at a dramatic rate; 13% of the population was age ≥ 65 years in 2010.[6] By 2030, nearly 20% of adults are expected to be in this age range, and the number of people age > 65 years is projected to double by 2050. The most rapidly increasing segment of the population is people

age ≥ 85 years; they made up 14% of the population age ≥ 65 years in 2010 and are projected to make up > 21% of this population by 2050.

Underrepresentation in Research

Multiple studies have documented the underrepresentation of older adults in cancer research. Underrepresentation is occurring in trials conducted to achieve US Food and Drug Administration (FDA) approval of new drugs, biologics, and devices as well as in federally funded research.

The proportion of older adults participating in FDA registration trials is historically low, as Talarico and Pazdur[7] found in an analysis of 28,000 research participants from 55 trials conducted between 1995 and 2002. Specifically, only 36% of trial participants were age ≥ 65 years, compared with 60% of the overall patient population; 20% of trial participants were age ≥ 70 years, compared with 46% of the overall patient population; and 9% of trial participants were age ≥ 75 years, compared with 31% of the overall patient population.

A Government Accountability Office study reviewed 36 new drug applications from 2001 to 2004.[73] Of the 28 applications reporting the number of older adults participating in trials, only 33% of the participants were age > 65 years. More recently, Scher and Hurria[8] reviewed the geriatric use sections of drug package inserts for 24 drugs approved for cancer treatment between 2007 and 2010. Only 33% of the participants were age ≥ 65 years, compared with almost 60% of the cancer population in this age range.

Similarly, low numbers of older adults participate in trials sponsored by the NCI Cooperative Group Program (now called National Clinical Trials Network).[9-14] Hutchins et al,[10] for example, analyzed enrollment of > 16,000 older adults in Southwest Oncology Group trials between 1993 and 1996. Twenty-five percent of the trial participants were age ≥ 65 years, compared with 63% of the patient population with cancer. When the age cutoff was set at 70 years, older adults made up 13% of research participants, compared with 47% of the patient population.

Lewis et al[11] evaluated the participation of older adults in NCI-sponsored treatment trials from multiple cooperative groups from 1997 to 2000. Of the 59,000 research participants in 495 trials, 32% were older adults, compared with > 60% of patients with cancer. There is limited evidence that participation of older adults in NCI-sponsored trials is improving over time. Data from the NCI show that the percentage of older adults enrolled onto cooperative group trials has remained flat at just > 20% between 2001 and 2011.[15]

Clinical Implications

Older adults respond differently to cancer treatments than younger people. This is partly attributable to age-associated physiologic changes, such as alterations in organ function. It is also influenced by the higher incidence of comorbidities and use of concomitant medications in older adults, which may interact with cancer treatments. According to the Centers for Disease Control and Prevention, approximately 80% of older adults have one chronic condition, and 50% have ≥ two.[16] These factors make older adults more sensitive to toxicity and adverse effects resulting from treatment. In addition, the treatment of older adults is complicated by the fact that there is great heterogeneity in their health. Chronologic age is an inadequate characterization of older adults' health status. Consideration of patients' functional age more accurately accounts for the genetic, lifestyle, and environmental factors that contribute to overall health status.

The underrepresentation of older adults in clinical trials means that clinicians have less evidence on how to treat the majority of patients with cancer. Clinicians and patients are forced to extrapolate from trials conducted in younger, healthier populations when developing treatment plans.[17-19] This has created a dearth of knowledge regarding the risk of toxicity in the average older patient. In addition, key end points of importance to older adults (eg, functional independence) are often not captured or reported.[20,21]

The lack of evidence on how to treat older adults is contributing to systematic differences in their treatment. Clinicians are uncertain whether all older adults are able to tolerate and benefit from cancer therapy.[22-25] Older patients receive chemotherapy less frequently than recommended by clinical practice guidelines, which could contribute to suboptimal health outcomes.[26-35]

RECOMMENDATIONS

ASCO makes five overarching recommendations for improving the evidence base for treating older adults with cancer, which build and expand on the recommendations in the IOM quality report. Table 1 summarizes these recommendations.

Recommendation 1

Use clinical trials to improve the evidence base for treating older adults. There are opportunities in clinical trials to improve the evidence base for treating older adults. Overly restrictive eligibility criteria in many trials limit the accrual of older adults.[11,19,36-39] For example, Bellera et al[39] reviewed clinical trial participation of older adults with non-Hodgkin lymphoma in 87 trials published in Medline between 2005 and 2011; > 25% of the trials directly excluded patients age > 65 years, and 54% indirectly excluded older adults through selective eligibility criteria. Common eligibility criteria in trials that lead to the exclusion of older adults include performance status, comorbid conditions, concomitant medication usage, and delayed diagnoses.

There is growing recognition that eligibility criteria in clinical trials could be relaxed without compromising scientific rigor.[19,40] From 1999 to 2005, the median number of eligibility criteria per trial increased from 31 to 49.[41] In addition, it is estimated that only 20% to 40% of patients treated at cancer centers are eligible to participate in

Table 1. Recommendation Goals

Recommendation
To improve the conduct of research
Use clinical trials to improve evidence for treating older adults with cancer
Leverage research designs and infrastructure for generating evidence on older adults with cancer
To improve the research environment
Increase FDA authority to incentivize and require research involving older adults with cancer
Increase clinicians' recruitment of older adults with cancer to clinical trials
Use journal policies to improve researchers' reporting of age distribution and health risk profiles of research participants

Abbreviation: FDA, US Food and Drug Administration.

clinical trials, primarily as a result of stringent eligibility criteria.[42] A 2010 IOM report recommended the development of eligibility criteria that allow the broadest participation possible.[43] Members of the ASCO Cancer Research Committee have also urged researchers and funders to carefully consider the necessity of individual eligibility criteria.[43a] Making eligibility criteria less stringent would speed up accrual, lead to more generalizable research, and improve identification of toxicities.[43,44]

Gathering additional data elements in clinical trials would also help improve the evidence base.[45] The health of older adults is heterogeneous[21]; however, little information is routinely captured about older adults who enroll onto trials aside from their chronologic age and performance status. The IOM quality report recommended that the NCI work with other stakeholders, like ASCO, to develop a common set of data elements to be collected by researchers in all trials.[1] Including elements from the geriatric assessment domains (eg, functional status, comorbid medical conditions, psychological state, cognitive function, nutritional status, social support) in these common data sets would help identify which older adults are most likely to benefit or not from treatment, because factors other than age are crucial to making these assessments.[46-53] Clinical trials conducted by the cooperative groups have documented that it is feasible to collect geriatric assessment data in a timely and efficient manner using existing tools.[54]

Similarly, there is substantial information to be gained from tumor specimens collected during clinical trials.[5] Tumors in older adults can be biologically different from those in younger populations.[31,55-59] For example, older adults are more likely to have hormone receptor–positive breast tumors than younger adults.[59] Requiring researchers to report the age distribution of samples studied in trials in which tumor specimens are collected would improve clinicians' understanding of how aging affects cancer biology.

Finally, the NCI should take a leadership role in ensuring that funders of cancer research, including the NIA and National Institutes of Health (NIH), encourage and incentivize increased involvement of older adults in clinical trials. Various approaches to fulfilling this role include creating targeted funding opportunities to support research involving older adults and including experts in geriatrics and geriatric oncology on review panels.

Action Items

- Regulatory agencies, funders of cancer clinical research, and researchers should carefully consider whether there is evidence supporting limitations to eligibility criteria based on age, performance status, or comorbid conditions. Researchers should provide a rationale, informed by input from experts in aging and geriatric oncology, when trials include eligibility criteria that are restricted based on these factors.
- The NCI, FDA, and other organizations developing common sets of data elements for researchers to collect in clinical trials should include measures from the geriatric assessment domains.
- Funders of cancer clinical trials in which tumor specimens are studied should require researchers to report on the age distribution of samples studied and whether this is reflective of the age distribution of the population enrolled onto the trial or the population with the disease overall.
- The NCI should collaborate with the NIA, NIH, and other funders of cancer clinical research to encourage and incentivize research including older adults.

Recommendation 2

Leverage research designs and infrastructure to improve the evidence base for treating older adults. Different study designs are appropriate for answering various types of questions, and researchers should choose the design most appropriate for the question of interest.[60-62] A recent U13 conference reviewed the benefits and limitations of various study designs for improving the evidence base for older adults, including randomized clinical trials, prospective cohort studies, embedded studies, and single-arm trials (Table 2).[15]

There are also several innovative trial designs, such as extended design trials and adaptive trials, which could improve the generation of evidence on older adults.[15] Extended design trials, for example, allow researchers to examine the age distribution of patients in the superior arm of a trial after the results have been reported. If the superior arm fails to accrue a sufficient number of older adults to draw conclusions, researchers reopen it to accrue a sufficient number.[15] Appropriately using the full range of trial designs to fill knowledge gaps could improve the evidence base guiding the treatment of older adults.

Comparative-effectiveness research (CER) is another effective method for developing the evidence base for treating older adults. CER is defined as "the generation and synthesis of evidence that compares the benefits and harms of alternative methods, to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care."[60(p13)] To leverage CER to improve the evidence base for treating older adults, the IOM quality report recommends that funders require researchers "to include a plan to study a population that mirrors the age distribution and health risk profile of patients with the disease."[1(p12)] This would further the central goal of CER: gathering data to inform real-world clinical decisions.

CER often depends on database research to answer important clinical questions. There are multiple databases with information on patients with cancer, including learning health care systems that merge data from large numbers of electronic health records, such as the ASCO CancerLinQ, as well databases that rigorously collect data, such as the SEER-Medicare database and cancer registries. A major advantage of research using these information sources is that researchers have access to data from large, diverse populations, including older adults, individuals with comorbidities, people using concomitant medications, and those who are in the oldest age ranges. Database research also produces results quickly and inexpensively. However, the data are not always collected systematically, creating the potential for bias or erroneous conclusions. To leverage databases to inform the treatment of older adults, it will be important that databases collect and store relevant information (eg, measures from geriatric assessment domains) and that they support appropriate analyses.

Coverage with evidence development (CED) is also a strategy for collecting clinical evidence on older adults.[63,64] Sponsors of new medical products currently have few incentives to conduct additional research after achieving insurance coverage for their products.[65] Under CED, payers cover the cost of a treatment while additional research is conducted.[66] This is unlike the more traditional research paradigm,

Table 2. Opportunities in Geriatric Oncology Clinical Trial Designs

Design	Description and Characteristics	Potential Objectives and Outcomes	Advantages	Limitations and Vital Considerations
RCT	Gold standard of clinical trial design; participants randomly assigned to treatment arms Study design for generating evidence in older adults: accrue only older adults or accrue patients of all ages but stratify enrollment into age groups representative of distribution of individuals with disease Adaptive (Bayesian) design: trial design is modified as study proceeds based on interim data analysis; randomization ratio can be altered by shifting patients to more effective treatment arm and eliminating underperforming arm	Compare efficacy and tolerability of different treatments; develop novel end points	Excellent for direct comparison of different regimens	Requires large sample sizes; is costly and time intensive; lack of end points tailored to geriatric population In trials stratified by age: slow accrual because of enrollment of specific age strata
Prospective cohort study	Assesses treatments already approved by FDA Cohort can be defined by host, tumor, or treatment factors Observational (no randomization) Hypothesis driven	Identify patterns of care; understand decision making; determine toxicity and feasibility of delivering specific therapies	Generalizable findings; provides insight into patterns of care and decision making	Lack of randomization; significant data management resources required to capture drug-dosing and toxicity data
Embedded study (correlative or ancillary study)	Measures of interest to geriatric oncology research are included within infrastructure of parent study (eg, GA domains)	Use GA to describe cohort; use GA in longitudinal follow-up to understand impact of therapy; identify characteristics of patients at high risk for toxicity	Baseline characterization of geriatric population in study; ability to identify baseline predictors of treatment tolerance and/or longitudinal declines in function	Parent study may not be targeted to older adults, thus limiting sample size of older patients If participation in embedded study is optional, patients may not be representative of entire cohort and/or adequate sample size of older adults may not accrue
Single-arm trial	Gold standard for phase II trials No randomization All patients receive treatment under study	Evaluation of efficacy of drug for which there are limited data for older adults Identification of predictors of toxicity based on GA variables or biomarkers Understanding of age-related changes in pharmacokinetics and pharmacodynamics of therapeutics	Qualification of novel end points Fills gaps in knowledge regarding efficacy, feasibility, and toxicity of drugs that have been understudied in older adults	No comparison arm
Extended trial	Addition of cohort of older patients to superior treatment arm or RCT	Determination of tolerability of treatment in older adults	Trial infrastructure in place Easier accrual of older patients because efficacy of treatment has been demonstrated Provides additional data on tolerability of treatment in older patients	No precedent exists for reopening study several years after closure No data regarding efficacy of treatment from inferior arm in older adults

NOTE. Data adapted.[15]
Abbreviations: FDA, US Food and Drug Administration; GA, geriatric assessment; RCT, randomized controlled trial.

where industry covers treatment costs in trials. Clinical trials conducted under CED programs are likely to be more generalizable, given that payers are interested in supporting research that will inform coverage decisions for their insured populations.

The Centers for Medicare and Medicaid Services (CMS), the major insurer of older adults, employed CED in oncology in 2005 by covering the off-label use of several chemotherapy treatments for colorectal cancer in specific NCI-sponsored trials.[67] Medicare should be highly motivated to participate in additional CED programs in oncology, given the difference between the average trial participant and the average Medicare beneficiary, who is older and less healthy.[18] Moreover, previous additions to the coverage of clinical trials by Medicare have increased the number of older adults participating in research.[68]

Action Items

- Researchers and funders of cancer clinical research should use the full range of research designs, including innovative trial designs, to fill knowledge gaps in the treatment of older adults with cancer.
- Funders of CER should require researchers evaluating the role of a standard or novel cancer treatment to include a plan to study a population that mirrors the age distribution and health risk profile of patients with the disease.
- Developers of research and clinical databases should ensure that their systems collect geriatric assessment data and have the functionality to support studies designed to improve the evidence base supporting the treatment of older adults with cancer.
- The CMS should use its coverage with evidence development authority to cover the off-label use of marketed drugs in select cancer clinical trials. The CMS should work with the NIH, patients, and researchers to prioritize trials for this additional coverage.

Recommendation 3

Increase the authority of the FDA to incentivize and require research including older adults. The FDA has limited authority to require sponsors of new treatments to test their products in older adults. Manufacturers are required to report their clinical trial results by age and include a geriatric use subsection on their product labels.[69,70] The FDA has also issued guidance that encourages, but does not require, sponsors to generate evidence on the effectiveness of their products in older adults.[71,72]

Despite these policies, older adults are rarely included in registration trials.[7,8,73] Moreover, the lack of information included in the geriatric use section of product labels has limited impact on the ability of manufacturers to market and sell their products to older adults. Only approximately half of drugs commonly prescribed to older adults contain precautionary information in the geriatric use section of their labels.[74] Manufacturers typically comply with this labeling requirement by noting that their products were tested in insufficient numbers of older adults to determine whether the products are likely to produce higher risks for older adults.

Given that the current regulatory approach of the FDA does not generate actionable information on the therapeutic effect of new treatments in older adults, changing the requirements and incentive structure for new treatments is required. Specifically, the FDA should have authority to require a sponsor to outline a plan to test its products in older populations. The FDA could issue a waiver if a product is unlikely to benefit older adults. Companies could meet this requirement through postmarketing trials, so products that are ready for approval in the general population are not kept off the market.

The FDA should also have the authority to create incentives for manufacturers to test their products in older adults. This incentive-based approach could be extended to drugs for other diseases that also occur frequently in older adults. The IOM quality report recommends rewarding companies for conducting clinical trials of new cancer treatments in older adults by providing them with 6 months of patent extensions, as modeled after the pediatric market exclusivity incentive.[1] There is substantial evidence of the success of the pediatric market exclusivity program at incentivizing research in children.[75,76]

There are also other examples of incentives that successfully encourage manufacturers to conduct research on specific topics or in specific populations, which could serve as models for a new incentive program for research in older adults: (1) the FDA Amendments Act of 2008 includes transferable vouchers for expedited review for companies developing new drugs to treat tropical diseases, (2) the Affordable Care Act includes multiple incentives to encourage manufacturers to develop biologic drugs, (3) the Orphan Drug Act provides market exclusivity for drugs treating rare diseases, and (4) the Hatch-Waxman Act includes incentives for both brand-name and generic drug manufacturers.[76] Although market exclusivity is the core approach to motivating manufacturers to conduct research, other types of incentives, such as prizes and government research and development contracts, can also be effective.[77]

The FDA should have flexibility in designing an appropriate incentive program to encourage research involving older adults. The program should be informed by previous incentive programs and narrowly tailored to achieve the desired outcome of generating the needed evidence. The authorizing law should also require an evaluation of the impact of the program on public health, include a mechanism that allows the FDA to modify the incentive based on the evaluation, and place limits on the compensation available to manufacturers. Moreover, it will be important that both the incentive program and any new requirements be harmonized with the European Medicines Agency (EMA) procedures.

In addition, the FDA should enhance the aging expertise on its advisory boards as it implements these new programs. Part of the EMA geriatric strategy included forming a geriatric expert group to advise the EMA and its scientific committees on relevant issues.[78] In the United States, the FDA Oncology Drug Advisory Committee is the most logical place to increase geriatric expertise. This committee is charged with reviewing and evaluating data concerning the safety and effectiveness of cancer treatments. It consists of 13 voting members from various fields but currently does not require a member with geriatric or aging expertise.[79] Including geriatric expertise would better ensure that manufacturers are submitting the appropriate data on the safety, efficacy, and dosing of their products in older adults.

Action Items

- Congress should provide the FDA authority to require that a drug or biologic marketing application contain a plan to gather data and develop recommendations on safety, efficacy, and dosing in older adults.
- Congress should grant the FDA authority to create incentives for companies that conduct clinical trials of new cancer treatments in older adults.
- The FDA should include experts in aging and geriatric oncology on its advisory boards to provide scientific advice on the development and assessment of novel agents and emerging federal policies.

Recommendation 4

Increase clinician recruitment of older adults to clinical trials. The biggest predictor of whether a patient decides to enroll onto a clinical

trial is whether a clinician has discussed and recommended participation. Thus, clinicians can be a major barrier to older adults' participation in research.[7,9,36,37,80] Although there is no evidence that enrollment of older adults onto clinical trials is associated with increased risk of harm over standard therapy,[11,14] clinicians regularly cite concerns about drug toxicity and the impact of treatment as reasons not to enroll older adults onto trials.[7,9,36,37] Clinicians' decision to offer trial participation to patients is often influenced by patients' chronologic rather than functional age.[81-86]

Nevertheless, multiple studies have found that older adults are as willing to participate in trials as younger adults when given the opportunity.[84,86,87] Older adults also generally have positive attitudes toward clinical trials.[88] Given these data, educational programs will be necessary to reduce clinicians' reluctance to enroll older adults onto trials. In addition, trial sponsors should avoid distributing educational materials that may discourage clinicians from enrolling older patients onto trials.

Increasing reimbursement for clinicians who enroll patients onto clinical trials would also improve recruitment. An IOM report concluded that the current reimbursement system fails to recognize the extra time and effort it takes to enroll patients onto trials, such as the time required to find applicable trials, explain trials to patients, and obtain informed consent.[43] There are also extra data collection and documentation and regulatory requirements for clinicians whose patients participate in research.[88] One study found that clinicians spend, on average, 4 hours enrolling patients onto trials, and some of these patients ultimately decide not to participate.[89] The additional uncompensated time and effort required for trial enrollment is particularly burdensome for clinicians enrolling older adults, given the increased challenge of identifying appropriate trials for this population, some older adults' heightened toxicity risks, and older adults' potential for cognitive impairments, which must be assessed to determine whether patients can provide informed consent.

Action Items

- Professional societies should develop and promote educational materials for clinicians and researchers to encourage greater recruitment of older adults to clinical trials.
- The American Medical Association should establish new current procedural terminology (CPT) codes to reimburse clinicians who offer older patients the opportunity to participate in clinical trials, enroll them onto these trials, and conduct management and follow-up of these patients for the additional time and effort involved. These CPT codes should be reimbursed by Medicare, Medicaid, and third-party payers.

Recommendation 5

Use journal policies to incentivize researchers to consistently report on the age distribution and health risk profiles of research participants. Researchers are currently collecting substantial data about older adults that are not being analyzed or reported. Thus, information that could inform clinical practice at little additional cost is not being reported. Kumar et al,[14] for example, reviewed 345 completed phase III clinical trials conducted by five cooperative groups for participation of older adults. They found that 57% of the trials did not stratify the results by age, and only 12% of trials stratified by age $\geq$ 65 years. This represents an easily addressed, missed opportunity to identify differences in safety, efficacy, and dosing associated with age. Using journal policies could improve researchers' reporting of data relevant to the treatment of older adults.

Action Items

- Require authors to submit and report the detailed age distribution (by decade) of the population included in the study, not just the age ranges of population, and data analyses that could potentially yield valuable age-related information, including age-based analyses of response, benefit, and toxicity.
- Include geriatric oncology experts in the pool of editorial board members who serve as peer reviewers of manuscripts.
- Instruct peer reviewers to consider whether the authors have adequately reported the age distribution of the population included in the study, the generalizability of the results to the population with the disease, and data analyses that could potentially yield valuable age-related information.

DISCUSSION

This article lays out a multipronged approach to improving the evidence base for treating older adults with cancer. Some of the recommendations are achievable in a short timeframe. Others will require longer-term commitments and the collaboration of multiple stakeholders involved in clinical research. Given the rapidly aging population, this is a crucial time to act to ensure all patients with cancer receive high-quality, evidence-based care.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

AUTHOR CONTRIBUTIONS

Manuscript writing: All authors
Final approval of manuscript: All authors

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Improving the Evidence Base for Treating Older Adults With Cancer: American Society of Clinical Oncology Statement

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Appendix

American Society of Clinical Oncology Recommendations: Improving the Evidence Base for Treating Older Adults With Cancer

Recommendation 1

Use clinical trials to improve the evidence base for treating older adults with cancer.

Action Items

- Regulatory agencies, funders of cancer clinical research, and researchers should carefully consider whether there is evidence supporting limitations to eligibility criteria based on age, performance status, or comorbid conditions. Researchers should provide a rationale, informed by input from experts in aging and geriatric oncology, when trials include eligibility criteria that are restricted based on these factors.
- The National Cancer Institute (NCI), US Food and Drug Administration (FDA), and other organizations that are developing common sets of data elements for researchers to collect in clinical trials should include measures from the geriatric assessment domains.
- Funders of cancer clinical trials in which tumor specimens are studied should require researchers to report the age distribution of samples studied and whether this is reflective of the age distribution of the population enrolled onto the trial and the population with the disease overall.
- The NCI should collaborate with the National Institute on Aging, National Institutes of Health, and other funders of cancer clinical research to encourage and incentivize research involving older adults.

Recommendation 2

Leverage research designs and infrastructure to improve the evidence base for treating older adults with cancer.

Action Items

- Researchers and funders of cancer clinical research should use the full range of research designs, including innovative trial designs, to fill knowledge gaps in the treatment of older adults with cancer.
- Funders of comparative-effectiveness research should require researchers evaluating the role of a standard or novel cancer treatment to include a plan to study a population that mirrors the age distribution and health risk profile of patients with the disease.
- Developers of research and clinical databases should ensure that their systems collect geriatric assessment data and have the functionality to support studies designed to improve the evidence base supporting the treatment of older adults with cancer.
- The Centers for Medicare and Medicaid Services should use its coverage with evidence development authority to cover the off-label use of marketed drugs in select cancer clinical trials. The Centers for Medicare and Medicaid Services should work with the National Institutes of Health, patients, and researchers to prioritize trials for this additional coverage.

Recommendation 3

Increase the authority of the FDA to incentivize and require research involving older adults with cancer.

Action Items

- Congress should provide the FDA authority to require a drug or biologic marketing application to contain a plan to gather data and develop recommendations on safety, efficacy, and dosing in older adults.
- Congress should grant the FDA authority to create incentives for companies that conduct clinical trials of new cancer treatments in older adults.
- The FDA should include experts in aging and geriatric oncology on its advisory boards to provide scientific advice on the development and assessment of novel agents and emerging federal policies.

Recommendation 4

Increase clinician recruitment of older adults with cancer to clinical trials.

Action Items

- Professional societies should develop and promote educational materials for clinicians and researchers to encourage greater recruitment of older adults to clinical trials.
- The American Medical Association should establish new common procedural terminology codes to reimburse clinicians who offer older patients the opportunity to participate in clinical trials, enroll them onto these trials, and conduct

management and follow-up of these patients for the additional time and effort involved. These codes should be reimbursed by Medicare, Medicaid, and third-party payers.

Recommendation 5

Use journal policies to incentivize researchers to consistently report the age distribution and health risk profiles of research participants.

Action Items

- Require authors to submit and report the detailed age distribution (by decade) of the population included in the study, not just the age ranges of population, and data analyses that could potentially yield valuable age-related information, including age-based analyses of response, benefit, and toxicity.
- Include geriatric oncology experts in the pool of editorial board members who serve as peer reviewers of manuscripts.
- Instruct peer reviewers to consider whether the authors have adequately reported the age distribution of the population included in the study, the generalizability of the results to the population with the disease, and data analyses that could potentially yield valuable age-related information.