

Participation of Patients 65 Years of Age or Older in Cancer Clinical Trials

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Purpose: Although 61% of new cases of cancer occur among the elderly, recent studies indicate that the elderly comprise only 25% of participants in cancer clinical trials. Further investigation into the reasons for low elderly participation is warranted. Our objective was to evaluate the participation of the elderly in clinical trials sponsored by the National Cancer Institute (NCI) and assess the impact of protocol exclusion criteria on elderly participation.

Patients and Methods: We conducted a retrospective analysis using NCI data, analyzing patient and trial characteristics for 59,300 patients enrolled onto 495 NCI-sponsored, cooperative group trials, active from 1997 through 2000. Our main outcome measure was the proportion of elderly patients enrolled onto cancer clinical trials compared with the proportion of incident cancer patients who are elderly.

Results: Overall, 32% of participants in phase II and III clinical trials were elderly, compared with 61% of patients with incident cancers in the United States who are elderly.

The degree of underrepresentation was more pronounced in trials for early-stage cancers than in trials for late-stage cancers ($P < .001$). Furthermore, protocol exclusion criteria on the basis of organ-system abnormalities and functional status limitations were associated with lower elderly participation. We estimate that if protocol exclusions were relaxed, elderly participation in cancer trials would be 60%.

Conclusion: The elderly are underrepresented in cancer clinical trials relative to their disease burden. Older patients are more likely to have medical histories that make them ineligible for clinical trials because of protocol exclusions. Insurance coverage for clinical trials is one step toward improvement of elderly access to clinical trials. Without a change in study design or requirements, this step may not be sufficient.

J Clin Oncol 21:1383-1389. © 2003 by American Society of Clinical Oncology.

CANCER WAS second only to heart disease as a leading cause of death in 1999.¹ The elderly (people aged 65 years or older) account for 61% of all new cancer cases and 70% of all cancer deaths,² and it is estimated that they have 11 times the cancer risk of people under the age of 65 years.² By 2030, approximately 20% of the United States population will be aged 65 years or older.³ Consequently, cancer care will become increasingly important.

Patients with cancer are living longer and experiencing better quality of life as a result of advances in cancer care. Clinical studies have resulted in curative treatments for leukemias, lymphomas, and germ cell tumors and decreased morbidity and mortality from colorectal and breast cancer.^{4,5} Other studies have found better ways of caring for cancer patients, minimizing side effects, and reducing invasive procedures.^{6,7} It is important that cancer clinical trials enroll a representative sample of patients to ensure that the results of these trials are applicable to all those with cancer.

Federal laws require that cancer trials enroll representative samples of women and members of minority groups.⁸⁻¹¹ These laws may have had some success; several studies indicate that women and minorities are proportionately enrolled onto National Cancer Institute (NCI)-sponsored, cooperative group treatment trials,¹²⁻¹⁴ whereas other studies disagree.¹⁵ In contrast, research indicates that the elderly are underrepresented in cancer clinical trials.¹⁵⁻¹⁸

A study of Southwest Oncology Group clinical trials active between 1993 and 1996 found that, although 63% of United States cancer patients were over 65 years old, the elderly comprised only 25% of trial participants.¹⁸ However, this study evaluated elderly participation using data from only one coop-

erative group. Furthermore, the investigators did not evaluate whether elderly participation differed by phase of the trial or stage of disease, or investigate the reasons for the underrepresentation among the elderly. Recent federal efforts have focused on expanded Medicare coverage for clinical trials. To assess the likely impact of improved insurance coverage, it is important to determine the numerous factors that may affect the representation of elderly persons in cancer clinical trials.

This article evaluates the participation of the elderly in NCI-sponsored cancer treatment trials active from 1997 through 2000 using data from multiple cooperative groups. We examine the participation of elderly patients in clinical trials stratified by trial phase (II v III) and by stage of disease (early v late). Most important, we assess the impact of clinical trial protocol exclusions on elderly participation in trials.

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Supported in part by the National Cancer Institute, with additional funding from the Office of the Director, National Institutes of Health, and the National Science Foundation. This research was also sponsored in part by the Robert Wood Johnson Clinical Scholars Program and by the Veterans Affairs (VA) Ambulatory Care Fellowship in Health Services Research at the West Los Angeles VA Medical Center (J.H.L.).

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0732-183X/03/2107-1383/\$20.00

PATIENTS AND METHODS

Data Sources

We used three NCI databases: the Cancer Therapy Evaluation Program (CTEP),¹⁹ the Physician Data Query (PDQ),²⁰ and the Surveillance, Epidemiology, and End Results Program (SEER).²¹ The CTEP and the PDQ were used to detail the characteristics of NCI-sponsored clinical trials, including the age distribution of trial participants. The SEER data were used to compute national cancer incidence rates for the elderly, so that the proportion of patients enrolled onto clinical trials who were elderly could be compared with the corresponding proportion of the population with cancer.

The CTEP Database

CTEP is responsible for planning, assessing, and coordinating clinical trials. As the manager of the collaborative clinical trial groups, the CTEP is a data clearinghouse to which investigators report their progress with each protocol. The CTEP data include protocol identification numbers, trial phase, planned and actual trial accrual, date when the trial began to enroll patients, end date, and participation by age. Our study focused on 495 adult, phase II and III cancer treatment trials that were conducted by cooperative groups and enrolled patients between 1997 and 2000. We chose to evaluate only cooperative group trials because of the strict reporting requirements for the groups; the CTEP database is considered complete for cooperative group trials active in 1997 and beyond.

The PDQ Database

The PDQ database contains detailed protocol exclusion criteria for NCI-sponsored clinical trials. For each of the 495 trials in the study, we determined the cancer type and stage, planned trial duration, and protocol exclusion criteria. Appendix 1 details the specific exclusions that we defined for each category of protocol exclusion criteria. Strict exclusions were those protocol exclusion criteria that required normal or nearly normal laboratory values or organ system function, whereas moderate exclusions allowed for mildly abnormal values while still imposing restrictions.

To define functional status exclusions, we created a new performance score by matching the Karnofsky scores with the Eastern Cooperative Oncology Group (ECOG)/Zubrod scores.^{22,23} The majority of the protocols used the ECOG/Zubrod score, which assigns patients a score from 0 to 5 on the basis of their ability to carry on activities of daily living. A number of trials used the Karnofsky score, which rates functional status from 0% to 100% of normal health. Appendix 1 also provides a table relating our exclusion definitions to the ECOG/Zubrod and Karnofsky scales. We defined three levels of functional status restrictions. Each trial was coded to reflect the protocol requirement that participants be able to function at the specified level or better. Thus, a trial with the most restrictive functional status requirements would require participants to be ambulatory and able to work, whereas a trial with the most lenient functional status requirement would allow patients to enroll who were nonambulatory and had limited self-care capabilities.

Life expectancy requirements, where present, ranged from 1 month to 10 years. We categorized life expectancy criteria into the following two groups: protocols with life expectancy requirements of ≤ 6 months and those with requirements greater than 6 months. Age restrictions for minimum or maximum age were recorded. If a trial specified that enrollees must be postmenopausal, the minimum age restriction was recorded as 50 years. Other exclusions included the requirements that patients have no history of psychiatric problems specific to the elderly, such as organic brain syndrome, Alzheimer's disease, or senility; have no history of other neurologic or psychiatric disorders, other cancers, human immunodeficiency virus or AIDS, other severe disease, or active infections; and not be pregnant.

We stratified cancer trials by the stage of the cancer being treated to determine whether the elderly were more or less likely to be represented in trials for the treatment of early-stage or late-stage cancers. Appendix 2 details the stage categories used for each cancer type. In general, stage I and II cancers were considered early-stage cancers and stage III and IV cancers were considered late-stage cancers. Some protocols treated patients with varying stages of cancer that crossed over this division and, therefore, could not be classified.

The SEER Database

The SEER Program of the NCI is the most authoritative source of information on cancer incidence and survival in the United States.²¹ The SEER data are gathered from 11 tumor registries covering approximately 13.6% of the United States general population and 12.3% of the United States population age 65 years or older.^{24,25} The SEER program includes population-based information regarding cancer patient demographics, primary tumor type, morphology, stage at diagnosis, first course of treatment, and follow-up vital status.

To calculate the proportion of the United States population with each cancer type who were 65 years or older, we adjusted the incidence rates from the 1997 SEER data to reflect the proportion of elderly in the nation as a whole. We used 1998 data from the United States Census Bureau to determine the number of elderly and the total population in all of the counties represented in the 11 SEER registries. We then aggregated the number of new cases of cancer among the elderly and the total population by cancer type. We divided the aggregate numbers by the respective populations in the SEER areas to yield the SEER incidence rates for each cancer in both the elderly and the total population. Next, incidence rates for the elderly and the total population within SEER registry counties for each type of cancer were multiplied by the number of elderly and the total population within the United States to yield the number of new cases nationally for both groups. We then divided the national number of new cases of cancer among the elderly by the national number of new cases of cancer in the total population to calculate the estimated proportion of the total population diagnosed with cancer who were elderly. Proportions were calculated for 18 specific cancer types, for all cancer types combined, and for early- and late-stage cancers.

Statistical Analysis

We evaluated the distribution of elderly participants across trials and for trials stratified by cancer type, phase, and stage. We compared the participation rates with the proportions of the elderly in the United States population with each cancer type using one-sample binomial tests. Two tailed P values of .05 or less were considered to indicate statistical significance.²⁶

We used a weighted linear regression to examine the association between the proportion of elderly participants in each trial, as the dependent variable, and the year the trial opened, trial phase, and protocol exclusion criteria.²⁷ We forced indicator variables for cancer type and cancer stage, and their interactions, into the model to control for epidemiologic differences in age distribution across cancer types. Variables for the year the trial opened, trial phase, and protocol exclusion criteria were chosen for inclusion using a backward stepwise selection procedure set to retain only variables that were significant at the $P = .05$ level. Each trial was weighted by its total enrollment in the linear regression model.

The regression results were subjected to several regression diagnostics, including residual analysis and an examination of outliers. Furthermore, the regression findings were robust to alternative model specifications, including specifying the dependent variable as a logistic transformation of the proportion of participants in each trial who were elderly. We present the results on the basis of the model with the untransformed dependent variable for ease of interpretation.

Predictions

We used the regression results to predict the proportion of elderly in each cancer trial that would have been expected in the absence of protocol exclusion criteria. We used two prediction models. We first relaxed the protocol exclusions that were based on organ system abnormalities by setting the values of the indicator variables for these exclusions to 0 for all trials and using the parameter estimates to predict the proportion of elderly in each trial. In the second model, we relaxed both exclusions that were based on organ-system abnormalities and exclusions that were based on functional status limitations.

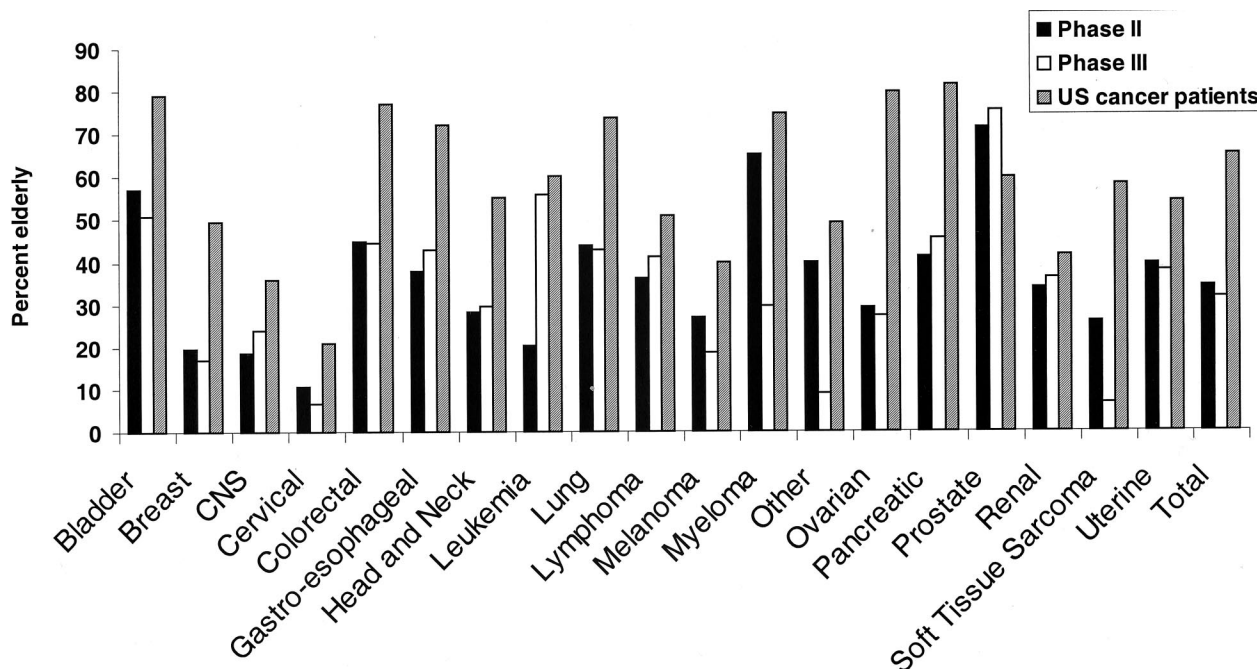


Fig 1. Comparison of elderly participation in phase II and III trials with percent of United States cancer patients who are elderly.

RESULTS

Descriptive Data

Overall, 32% of the participants in the clinical trials were elderly, compared with 61% of patients with incident cancers in the United States population who are age 65 years or older. Figure 1 shows the proportions of elderly patients in phase II and III trials for 18 cancer types compared with the proportions of

the United States population with each cancer type who are elderly. The elderly were significantly underrepresented ($P < .05$) in phase III melanoma trials; phase II CNS, gastroesophageal, renal, and soft tissue cancer trials; and phase II and III breast, cervical, colorectal, head and neck, leukemia, lung, and uterine cancer trials.

Table 1 lists the proportions of elderly patients in early- and late-stage cancer trials by cancer type compared with the

Table 1. Elderly Participation in NCI-Sponsored Cooperative Group Cancer Treatment Trials From 1997 Through 2000 by Cancer Stage*

Cancer Type	Early Stage			Late Stage		
	No. of Trials	% Elderly	Incidence Rate (%)†	No. of Trials	% Elderly	Incidence Rate (%)†
Bladder	2	57	78	6	51	81
Breast	25	18	49	20	20	48
CNS	4	11	6	25	22	31
Cervical	2	4	37	21	9	24
Colorectal	4	54	78	15	41	73
Gastroesophageal	4	42	75	11	39	66
Head and neck	0	—	59	22	29	48
Lung	13	48	75	46	42	70
Lymphoma	4	56	48	13	44	51
Melanoma	1	14	44	15	24	46
Ovarian	3	23	31	30	29	59
Pancreatic	1	40	81	10	45	72
Prostate	4	67	82	17	76	73
Renal	0	—	57	7	35	60
Soft tissue sarcoma	0	—	41	8	24	40
Uterine	5	38	56	23	43	64
Other‡	2	0	37	27	37	47
Above sites combined	74	25	57	316	41	65

Abbreviation: NCI, National Cancer Institute; CNS, central nervous system.

*Does not include 56 trials that treated patients with varying stages of cancer and, therefore, could not be classified as early or late.

†Incidence rate is the percentage of the population with each type and stage of cancer who are elderly. (Unavailable data for early-stage leukemias or myelomas; therefore, table excludes the 11 myeloma and 38 leukemia trials.)

‡Clinical trials classified as other treated the following disorders: adrenocortical tumors, AIDS-related sarcomas and lymphomas, amyloidosis, carcinoid tumors, germ cell tumors, granulocytopenia, hepatomas, mesotheliomas, mycosis fungoides, osteogenic sarcomas, penile tumors, testicular tumors, trophoblastic neoplasia, thymomas, urothelial tumors, vulvar tumors, and Waldenstrom’s macroglobulinemia.

proportions in the United States population with each cancer. (We excluded trials that could not be classified as early or late stage as well as trials for leukemia or myeloma.) The elderly were less underrepresented, relative to incidence rates, in trials for late-stage cancers than in trials for early-stage cancers ($P < .001$). For all cancer types, 25% of participants in trials for early-stage cancers and 41% of participants in trials for late-stage cancers were elderly. In the United States population, 57% of new cases of early-stage cancer and 65% of new cases of late-stage cancer occur in the elderly.

The majority of cancer trials prohibited participation by people with hematologic, hepatic, renal, or cardiac abnormalities (Table 2). More than 80% of the trials required participants to be either ambulatory and capable of work or capable of carrying out their activities of daily living independently. A minority of trials excluded individuals who had specific psychiatric diseases that are more common in the elderly, such as organic brain syndrome, Alzheimer's disease, or senility. Few trials had exclusions that were based on pulmonary disease, but most trials excluded individuals who had a history of another cancer.

Regression Analysis

Trials with exclusions on the basis of hypertension or cardiac, hematologic, or pulmonary function abnormalities enrolled lower proportions of elderly patients than trials without such exclusions (Table 3; Appendix 3). For example, all other things being equal, the proportion of elderly patients was 8.6% lower (95% confidence interval [CI], 5.2% to 12.0%) in trials that excluded patients with cardiac abnormalities than in trials that did not exclude these patients. Similarly, trials that excluded patients with functional status limitations enrolled lower proportions of elderly patients than trials that explicitly allowed patients with impaired functional status. For instance, all other things being equal, the proportion of elderly patients was 22.3% lower (95% CI, 15.5% to 29.2%) in trials that excluded patients with mild functional status impairment than in trials that did not exclude these patients. Interestingly, trials that did not specify any functional status exclusions enrolled lower proportions of elderly patients than trials that explicitly allowed patients with impaired functional status. Trials that specified life expectancy requirements enrolled slightly higher proportions of the elderly patients. Given the small number of trials with age restrictions, these were not found to be significantly associated with elderly enrollment.

The regression analysis also found that the proportion of elderly patients was 23.9% higher (95% CI, 14.5% to 32.2%) in trials for late-stage cancers than in trials for early-stage cancers or in trials that included multiple cancer stages. The phase of the trial was not associated with differences in elderly participation.

Predictions

When we relaxed the cardiac function, hypertension, hematologic, and pulmonary function exclusions, the overall predicted proportion of elderly patients increased to 46.7%. When we relaxed both the organ system and functional status exclusions, the overall predicted proportion of elderly patients increased to 59.7% (Fig 2).

Table 2. Protocol Exclusion Criteria Specified in 495 Phase II and III NCI-Sponsored Cooperative-Group Cancer Treatment Trials

Type of Exclusion	Phase II Trials (%)	Phase III Trials (%)	Aggregate Trials (%)
Hematologic			
Strict	21	27	23
Moderate	65	48	59
Any	86	75	82
Hepatic			
Strict	59	61	60
Moderate	28	21	25
Any	87	82	85
Renal			
Strict	53	43	49
Moderate	34	37	35
Any	87	80	84
Pulmonary			
Strict	1	1	1
Moderate	9	14	11
Any	10	16	12
Psychologic			
Broad	14	20	16
Specific*	3	3	3
Any	16	23	19
Functional status requirements†			
Ambulatory and able to work	19	30	23
Ambulatory and able to do ADLs‡	70	43	62
Nonambulatory with limited self-care	5	9	6
Any	94	82	91
Cardiac			
Congestive heart failure	41	47	43
Coronary artery disease	34	38	35
Conduction disease/arrhythmia	23	31	25
Hypertension	8	7	8
Life expectancy			
Life expectancy, \leq 6 months	20	7	16
Life expectancy, $>$ 6 months	21	26	23
Any	41	33	39
Age restriction, years			
Minimum age, 50 y	0.0	0.6	0.2
Minimum age, 75 y	0.3	0.0	0.2
Maximum age, 65 y	0.0	0.6	0.2
Maximum age, 70-99 y	0.2	1.8	0.8
Other			
Neurologic	16	12	15
No other cancer	88	91	89
Not pregnant	81	73	78
AIDS/HIV	14	13	14
Severe disease	23	28	25
Infection	40	34	38

Abbreviations: NCI, National Cancer Institute; ADLs, activities of daily living; HIV, human immunodeficiency virus.

*Specific psychiatric exclusions include organic brain syndrome, Alzheimer's Disease, and senility.

†The protocols required individuals to function at the level detailed or better.

‡ADLs require enrollees to be capable of all self-care, but they may be unable to carry out any work activities.

DISCUSSION

We found that the elderly are underrepresented in cancer clinical trials relative to the proportion of the cancer population who are elderly and that underrepresentation of the elderly is more pronounced in trials for early-stage cancers than in trials for late-stage cancers. We also found that protocol exclusion criteria that are based on organ-system abnormalities and func-

Table 3. Impact of Protocol Exclusions on Participation of the Elderly in Clinical Trials*

	Change in Elderly Participation (lower/higher)	
	%	95% CI
Organ system		
Abnormal cardiac function excluded	8.6†	5.2 to 12.0
Hypertension excluded	5.3†	0.8 to 9.7
Abnormal hematologic function excluded	14.1†	10.4 to 17.7
Abnormal pulmonary function excluded	9.3†	4.4 to 14.1
Functional status		
Mild functional status impairment excluded	22.3†	15.5 to 29.2
Moderate functional status impairment excluded	22.6†	15.9 to 29.3
No functional status exclusion specified	28.9†	22.4 to 35.5
Life expectancy		
Any specified life expectancy requirement	3.5‡	0.6 to 6.5
Adjusted R ²	0.653	

Abbreviation: CI, confidence interval.

*The dependent variable is the percent of elderly participating. Controlling for cancer site and stage and site-stage interactions.

†Percent lower.

‡Percent higher.

tional status limitations are associated with lower rates of elderly participation in cancer trials and almost fully explain the observed underrepresentation of the elderly in these trials relative to their burden of disease.

Although the elderly were underrepresented in the trials we evaluated, they comprised a larger proportion of clinical trial participants than previously reported. Expanding the analysis to all cooperative groups and focusing on the last 4 years narrowed the gap between the 61% of the cancer population who are

elderly and the previously reported 25% of cancer clinical trial participants who are elderly.¹⁸ Using the more comprehensive data, we found that 32% of patients in cancer trials were age 65 years or older.

We did not find a significant difference in elderly participation between phase II and phase III clinical trials. Phase II clinical trials are generally smaller, nonrandomized studies that evaluate both the toxicity and anticancer effects of therapies. Phase III trials build on the knowledge from the phase II trials and are generally randomized controlled trials comparing a new treatment or an investigational protocol to the standard of care.

This study is the first comprehensive study to summarize the protocol exclusion criteria that are used in cancer clinical trials and relate them to elderly participation.²⁸ Older patients are more likely to have medical histories and conditions that make them ineligible for cancer treatment trials that include protocol exclusions. Our prediction models demonstrate the substantial impact of restrictive protocol exclusion criteria on elderly participation.

Of course, protocol exclusion criteria are not arbitrary. For example, it is important that participants in trials that use nephrotoxic chemotherapies have normal renal function. Similarly, pulmonary and cardiac toxicity can be risks of cancer treatment, and it is reasonable for certain trials to require ample pulmonary or cardiac reserve for the patients to tolerate the therapy. Comorbidity also can affect survival, and elderly patients with comorbid conditions may be more likely to die of causes other than the cancer being treated, making treatment effects more difficult to detect.^{3,29} Nonetheless, protocol exclusion criteria that are based on comorbid conditions or functional

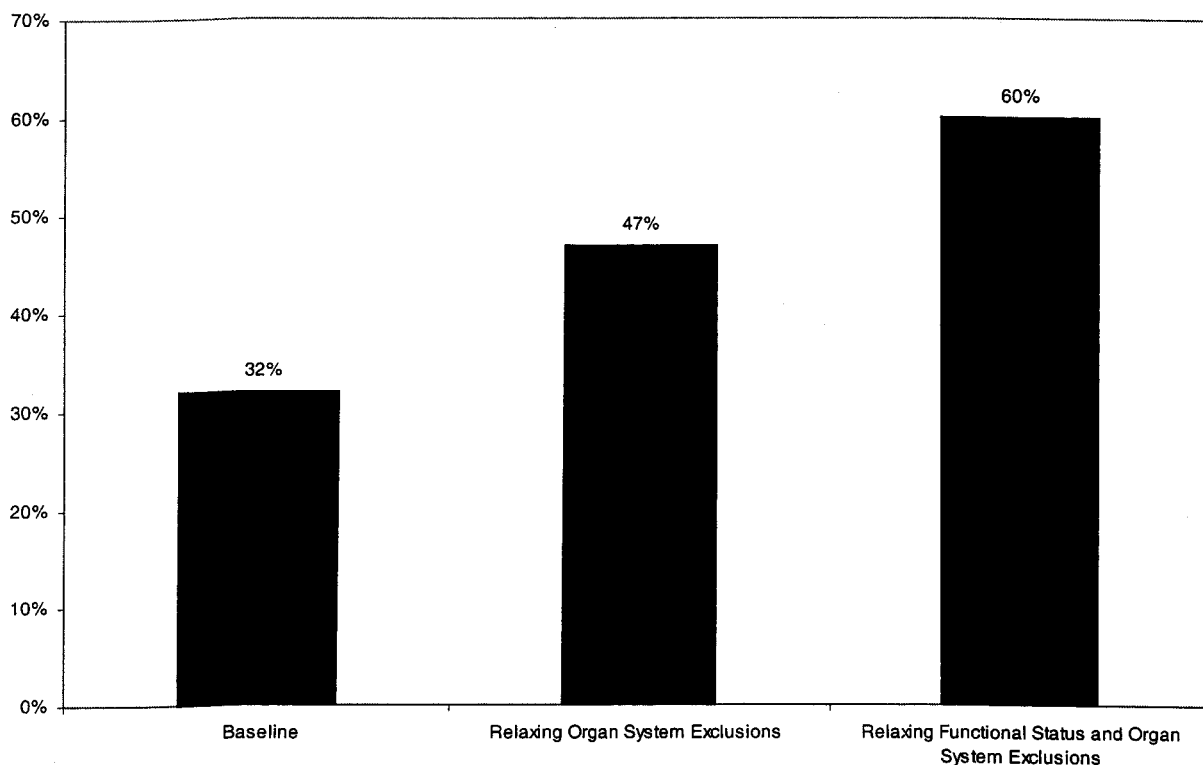


Fig 2. Predicted elderly enrollment when exclusion criteria are relaxed. Exclusions include cardiac function, hypertension, hematologic, and pulmonary function.

status limitations disproportionately disqualify older patients from clinical trials. When designing a clinical trial, investigators must examine each protocol exclusion and be certain that it is scientifically justified for a particular trial before including it in the protocol.

As the United States population ages a greater proportion of cancer patients will be elderly. Studies of many different cancers have demonstrated age-related differences in the natural history of cancer and in the effect of cancer treatment. For example, in prostate cancer, age has been found to be an independent predictor of distant metastases after treatment.³⁰ In non-Hodgkin's lymphoma, age greater than 65 years has been found to be a significant negative prognostic factor.³¹ Studies of leukemias have found that older patients do not tolerate intensive treatment as well as younger patients.^{32,33} In addition, specific biologic characteristics in older patients can be associated with poor outcomes,³⁴ and there is evidence that hematologic, cardiac, gastrointestinal, and neurologic toxicity related to chemotherapy may be more severe in older patients.³⁵ Therefore, to ensure that cancer trials develop and evaluate therapies for all patients with cancer, trials will need to enroll elderly patients in sufficient numbers.

It is legitimate to question whether cancer trials should recruit older subjects in proportion to their cancer incidence. Achieving such a goal would involve major redesign of investigative protocols and considerable expense. Furthermore, if the elderly with comorbidities are less likely than younger adults to benefit from certain therapies, increasing elderly participation in clinical trials could produce less-conclusive results with smaller treatment effects.

Even though proportionate participation of the elderly in trials may not be desirable or feasible, it is important to determine the factors that influence elderly participation in trials and to ensure that the elderly have access to trials. It may be necessary to design more trials that focus exclusively on elderly subjects or that address the treatment of cancer patients with specific comorbidities. Similarly, it may be important that certain cancer trials enroll elderly patients in sufficient numbers to allow for statistically meaningful subgroup analyses. More information is needed on the differential response to and tolerance of chemotherapies by age and in individuals with and without comorbidities.

Our study has several limitations. First, we did not have the data to determine the degree to which the protocol exclusions were followed. However, all of the trials in our sample were audited according to the CTEP guidelines.

Second, our regression analyses do not demonstrate that protocol exclusion criteria are causally related to lower elderly participation; rather, they reveal associations that in some cases may have alternative explanations. Our finding of an association between life expectancy requirements and higher elderly participation was unexpected. These trials may have been actively targeting older populations, and therefore, the investigators may have felt it important to specify life expectancy exclusions.

Despite this unexpected finding, it seems likely that most of the associations that we found between elderly participation and protocol exclusions on the basis of organ-system abnormalities or functional status limitations represent causal relationships.

Finally, our study did not assess the nonclinical factors that may influence elderly participation in cancer trials. For example, older patients may be less likely to seek out clinical trials¹⁶ and may be more inclined than younger patients to obtain treatment from their community physicians rather than transfer their care to academic medical centers or cancer centers. Differences in elderly persons' preferences for trials could be a result of differences in education, stronger relationships with primary care physicians, or difficulty getting to and from distant providers. The frequent visits required for aggressive cancer care or to participate in clinical trials may not be feasible for elderly persons who live alone or lack social supports. In addition, the elderly and their families may have preconceived notions about the potential benefits to elderly patients from participating in clinical trials or from aggressive cancer therapy.

Previous research indicates that investigators may be reluctant to enroll elderly patients in clinical trials.³⁶ This may be because of preconceived notions about the ability of the elderly to tolerate aggressive therapy. For example, the elderly have been found to be less likely to receive aggressive cancer treatment despite a lack of evidence that age is a risk factor for drug toxicity or surgical mortality.³⁷ Elderly breast cancer patients receive less aggressive care, independent of the presence of comorbidities.³⁸

The NCI has several initiatives in place to assess the impact of various factors that may affect the recruitment of older patients to clinical trials and to determine the effect of comorbidities on tolerance of cancer treatment.^{16,39} Future research should examine the preferences of the elderly regarding participation in trials, as well as the beliefs and behaviors of investigators regarding participation of the elderly in trials.

The results of our study indicate that recent federal policy to expand Medicare coverage for cancer clinical trials, by itself, is unlikely to substantially increase the level of elderly participation in cancer treatment trials. We found that protocol exclusions that are based on organ-system abnormalities and functional status limitations in NCI-sponsored trials disproportionately disqualify the elderly from participation and almost fully account for elderly patients' underrepresentation in trials relative to their cancer burden. Without a better understanding of the scientific justification for these exclusions, more trials focused on the elderly, or changes in study design or requirements, many cancer clinical trials may fail to provide the best possible evidence for treating elderly patients with cancer.

ACKNOWLEDGMENT

We thank Mary McCabe for her counsel. We also thank Nikhil Wagle for his assistance with data abstraction and Kris Parker for her assistance in preparing the article.

APPENDICES

The appendices are available online at www.jco.org.

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