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ORIGINAL REPORT

Patient Education Level As a Predictor of Survival In Lung Cancer Clinical Trials

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ABSTRACT

Purpose
To investigate the effect of socioeconomic status, as measured by education, on the survival of 1,577 lung cancer patients treated on 11 studies conducted by the Cancer and Leukemia Group B.

Patients and Methods
Sociodemographic data, including education, was reported by the patient at the time of clinical trial accrual. Cox proportional hazards model stratified by treatment arm/study was used to examine the effect of education on survival after adjustment for known prognostic factors.

Results
The patient population included 1,177 patients diagnosed with non–small-cell lung cancer (NSCLC; stage III or IV) and 400 patients diagnosed with small-cell lung cancer (SCLC; extensive or limited). Patients with less than an eighth grade education (13% of patients) were significantly more likely to be male, nonwhite, and older; have a performance status (PS) of 1 or 2; and have chest pain. Significant predictors of poor survival in the final model included male sex, PS of 1 or 2, dyspnea, weight loss, liver or bone metastases, unmarried, presence of adrenal metastases and high alkaline phosphatase levels among patients with NSCLC, and high WBC levels among patients with advanced disease. Education was not predictive of survival.

Conclusion
The physical condition of patients with low education who enroll onto clinical trials is worse than patients with higher education. Once enrolled onto a clinical trial, education does not affect the survival of patients with SCLC or stage III or IV NSCLC. The standardization of treatment and follow-up within a clinical trial, regardless of education, is one possible explanation for this lack of effect.

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INTRODUCTION

Evidence for the link between socioeconomic status (SES) and health/disease has accumulated over the years, mainly through the theoretical framework from the social determinants of health.[1,2] Several investigators have examined the statistically significant effect of income and education on survival in the general population.[1-5] The first of two explanations for this relationship is poverty in the form of material deprivation (eg, clean water and adequate nutrition). Alternatively, for rich countries such as the United States, the explanation given by Marmot[6] is that the relationship between income and survival is not the effect of poverty but the effect of relative differences in "opportunities for social participation, for leading a fulfilling and satisfying life, and for control over one's life." Social conditions including health practices, psychosocial characteristics of work (control, variety, and satisfaction), social support, and sense of control over the future are important in the determination of mortality. Much of the literature referenced earlier focuses on income; however, Marmot[6] notes that education may be an even better indicator of factors linked to social position that are important to health and survival.

In an often quoted article about the relationship between SES and the survival of cancer patients, Cella et al[7] reported that income and education were significant predictors of survival among patients treated for cancer on clinical trials conducted by the Cancer and Leukemia Group B (CALGB), a national cooperative group funded by the National Cancer Institute. That study showed that, after adjustment for known prognostic factors including cancer type, performance status, age, and protocol-specific prognostic factors, patients with annual incomes less than $5,000 and patients with only a grade school education had poorer survival than patients with higher SES treated on CALGB trials. The data used

in these analyses were drawn from eight CALGB studies conducted between 1977 and 1983 that involved 2,089 patients, including patients with lung cancer (n = 961), multiple myeloma (n = 577), gastric cancer (n = 231), pancreatic cancer (n = 174), breast cancer (n = 87), and Hodgkin's disease (n = 58).

Questions about the relationship between SES and cancer survival persist. Numerous articles have addressed the effect of various measures of SES on cancer survival.[8-29] However, inferences have not always been consistent because of differing research methodology, such as differences in the research question being asked (eg, impact of education on survival in the general population or impact in a clinical trial population), the patient population (eg, homogeneous or heterogeneous histology), the source of the data (eg, census, regulatory, Surveillance, Epidemiology, and End Results, or clinical treatment trial), and the measure of SES and its source (eg, patient reported or administrative databases).

For lung cancer, the reviewed literature is inconsistent relative to a relationship between SES and survival of patients. Eight publications that included or completely focused on patients with lung cancer were reviewed. Four articles focused on patient-reported measures of SES, including education,[17] education and income,[14,21] and occupation.[22] Two of these articles focused on a mixed cancer patient population, with Vigano et al's[14] advanced cancer patient population including 77 lung cancer patients and Stavraky et al's[17] population including 202 lung cancer deaths. Both articles reported that the relationship of SES-related variables with survival was not statistically significant. The remaining articles that focused on patient-reported measures of SES included patients with early-stage cancer.[21,22] Greenwald et al[21] reported that income, not education, was a significant predictor of survival among 125 lung cancer patients; however, Bouchardy et al[22] reported that SES based on occupation was not a significant predictor of long-term survival. Coleman et al[13] examined a population base of 3 million cancer patients, including approximately 150,000 lung cancer patients. Without adjustment for stage and other prognostic factors, this article showed that the survival patterns of rich and poor cancer patients were significantly different. After adjustment for known prognostic factors and comorbidity, Tammemagi et al[8] found no significant relationship between income estimated from census-tract data and survival among a heterogeneous population of 1,155 lung cancer patients from a cancer registry. Sowah et al[20] reported that income estimated from census tract data was not predictive of survival among 367 patients with non–small-cell lung cancer (NSCLC) overall; however, among patients with stage I disease, the relationship was statistically significant. Recently, Ou et al[19] presented similar results among 19,702 patients from the California Cancer Registry with stage I disease based on a composite measure stemming from census block data.

This report is part of a larger project the purpose of which is to examine a large database of Background Information Forms that CALGB has routinely collected between 1990 and 1998 and to validate the findings of Cella et al[7] concerning the relationship of education and survival within larger, homogeneous cancer patient populations that participated in CALGB clinical trials. This report focuses specifically on the relationship between education and survival among patients with NSCLC or small-cell lung cancer (SCLC) who participated in 11 CALGB clinical trials (CALGB 8831, 8931, 9532, 9033, 9130, 9235, 9430, 9431, 9534, 9730, and 9731).[31-43] The strength of this research is that it uses a measure of SES provided by the patient, explores the relationship between education and survival within relatively homogeneous patient groups, and has power (ie, sufficient patient numbers) to detect clinically important effect sizes within the unique context of clinical trials.

PATIENTS AND METHODS

CALGB Collection of Socioeconomic Data

The CALGB Psychiatry Committee (later renamed the Psycho-Oncology Committee) piloted the collection of socioeconomic data from a Background Information Form on two CALGB studies[30] and showed the feasibility of collecting such data for all variables except income. In the early 1990s, after completion of the feasibility study, CALGB initiated the collection of the Background Information Form on all active studies. Included among the data provided by the patient were education, race, and marital status. Education was presented as a multiple choice question with the following options: grades 1 to 8, grades 9 to 11, high school graduate, some college, junior college degree, college degree, some postcollege, or advanced degree. Income was not collected because of collection difficulties encountered in the feasibility study. In approximately 1998, CALGB discontinued the collection of the Background Information Form from all studies and limited its collection to studies specifically needing such data to answer the study's primary scientific questions. As of today, the Background Information Form has been collected from more than 18,000 patients on more than 140 studies, including more than 1,500 lung cancer patients. Survival data and baseline clinical data were obtained from the CALGB database and merged with the Background Information Form.

Patient Population

The analyses presented in this article are based on education and clinical data collected in 11 lung cancer studies coordinated by the CALGB. These studies[31-43] are listed in Table 1, along with data concerning accrual, patient eligibility, the availability of Background Information Form data, and the patient status (alive or dead) at last follow-up. The submission of the Background Information Form that collected data about the patient's education was required for all studies except for CALGB 9130 and 9033. For these two studies, the requirement to submit such data was instituted during the latter months of patient accrual. The results of all 11 studies, as well as details about treatment regimens administered, have been previously reported.[31-43] During the conduct of these clinical studies, the study chair reviewed the eligibility of the patients who were enrolled onto the study by participating institutions. The analyses contained in this article exclude those patients who were not originally eligible for the study and were excluded from the study's primary analysis.

Power Calculations

A priori power calculations were generated to determine whether clinically meaningful effects would be detectable with available data if they existed. Cella et al[7] reported that 31% of patients had only a grade school education and that their hazard ratio of death relative to patients with more than a grade school education was approximately 1.2. The current data set includes 1,577 lung cancer patients, of whom 1,491 are dead and 13.1% had only a grade school education (Tables 1 and 2). With a two-tailed log-rank test conducted at the $P = .05$ level of significance, a hazard ratio of 1.24 is detectable with 80% power in this sample.

Analytic Methods

Most patients on the studies considered in this project had a Background Information Form submitted. To guard against possible bias, the characteristics of patients (age, sex, race, performance status, and weight loss) who had a Background Information Form with education data were compared with the characteristics of all other patients accrued to these studies, including patients without a Background Information Form and patients with a Background

Table 1. CALGB Lung Cancer Studies (N = 11) From Which Patients Were Drawn

Disease, Stage, and Study	Treatment Arms	Enrollment Dates	No. of Patients Enrolled	No. of Patients Eligible	Eligible Patients With Education Data		No. of Deaths Among Eligible Patients With Education Data	Date of Last Follow-Up*
					No.	%		
Total lung			2,350	2,210	1,577	71	1,491	
NSCLC			1,616	1,505	1,177	78	1,127	
Advanced								
8931	Cisplatin, etoposide, placebo Cisplatin, etoposide, hydrazine	August 1989-February 1991	291	266	227	85	225	June 2000
9532	Vinorelbine, ifosfamide Paclitaxel, ifosfamide	September 1995-July 1996	100	93	81	87	74	October 2002
9730	Paclitaxel Paclitaxel, carboplatin	December 1997-January 2001	584	561	505	90	494	September 2004
9731	Paclitaxel	September 1997-April 1998	39	38	38	100	35	February 2002
Stage III								
8831	Vinblastine, cisplatin → RT → cisplatin, vinblastine Vinblastine, cisplatin → RT, carboplatin	August 1988-October 1989	91	85	73	86	67	October 2000
9130	Vinblastine, cisplatin → RT Vinblastine, cisplatin → RT, carboplatin	September 1991-November 1996	283	250	69	28†‡	64	October 2001
9431	Cisplatin, gemcitabine → cisplatin, gemcitabine, RT Cisplatin, paclitaxel → cisplatin, paclitaxel, RT Cisplatin, vinorelbine → cisplatin, vinorelbine, RT	January 1996-June 1998	187	172	149	87	136	February 2004
9534	Paclitaxel, carboplatin → paclitaxel, carboplatin, RT	August 1996-January 1999	41	40	35	88	32	July 2003
SCLC			734	705	400	57	364	
Limited								
9235	Etoposide, cisplatin → RT Etoposide, cisplatin → RT + carboplatin	August 1993-January 1999	319	307	247	80	213	October 2005
Extensive								
9033	Oral etoposide, IV cisplatin IV etoposide, IV cisplatin	February 1991-October 1993	319	306	74	24†‡	73	May 1997
9430	Cisplatin, topotecan, G-CSF Cisplatin, paclitaxel 230 mg/m^2, G-CSF Paclitaxel 230 mg/m^2, topotecan, G-CSF Paclitaxel 175 mg/m^2, topotecan, G-CSF	May 1995-June 1999	96	92	79	86	78	February 2002

Abbreviations: CALGB, Cancer and Leukemia Group B; NSCLC, non–small-cell lung cancer; RT, radiotherapy; SCLC, small-cell lung cancer; IV, intravenous; G-CSF, granulocyte colony-stimulating factor.
*The latest recorded date of death or date of last follow-up used to compute survival time among patients included in analyses.
†When CALGB 9033 and 9130 were originally activated, the submission of a Background Information Form to the CALGB Statistical Center was not a requirement.
‡Percent of eligible patients.

Information Form lacking education data, using Cochran-Mantel-Haenszel and Fisher's exact χ^2 tests and *t* tests.[44,45]

Survival time was defined as the period between the date of study enrollment and the date of death. For those patients who were censored in analyses, survival time was defined as the time between study entry and the date of last contact. The Kaplan-Meier product-limit estimator was used to describe the survival experience within patient subgroups defined by various prognostic factors.[46] Median survival estimates were generated using the estimator of Brookmeyer and Crowley.[47] The Cox proportional hazards model stratified by treatment arm/study was used to assess the relationship between survival and known prognostic factors.[48] Known clinical and sociodemographic predictors that were considered in analyses are listed in Table 2. If the relationship between an individual factor and survival was statistically significant in univariate analyses at the $P = .25$ level of significance, that factor was included in subsequent multivariable analysis using backwards elimination.[49] Interactions were also considered in analyses, including factor × histology (NSCLC or SCLC), factor × stage (advanced/extensive *v* other), and factor × histology × stage. Martingale and Schoenfeld residuals were used to assess the adequacy of the proportional hazards assumption.[50] Once a final multivariable clinical model was determined, factors describing the effect of education and interactions between education, histology, stage, and the model's strata were added to the Cox model. The Cox analysis described earlier was stratified by treatment arm/study to allow different nonproportional hazard rates for the various combinations of studies and treatment arms.

RESULTS

The analyses described in this report are based on the experiences of 1,577 lung cancer patients (Table 1). This patient cohort constitutes 67% of the patients originally accrued to the 11 lung cancer studies considered. A comparison of the characteristics of the 1,577 patients included in these analyses and the 633 other eligible patients accrued to these 11 studies showed no significant difference relative to age, sex, race, performance status, and weight loss.

Among the 1,577 patients are those with advanced NSCLC (851), inoperable stage III NSCLC (326), extensive SCLC (153), and limited SCLC (247). The majority of patients were male (66%), white (84%), over 59 years of age (61%), and had performance

Table 2. Characteristics of Patients With Lung Cancer and Survival Rates

Predictor	No. of Patients	%	No. of Patients Dead	Survival Time (months)		Hazard Ratio	95% CI	P (χ^2)
				Median	95% CI			
Sex								
Male	1,047	66	1,001	10.5	9.9 to 11.1			
Female	530	34	490	12.1	11.0 to 13.4	0.84	0.75 to 0.94	.0024
Race								
White	1,331	84	1,252	11.1	10.6 to 11.8			
Black	168	11	164	10.2	8.6 to 12.2	1.17	0.99 to 1.39	
Hispanic	40	3	40	9.2	6.8 to 13.3	1.13	0.82 to 1.56	
Other	38	2	35	9.4	7.4 to 14.6	1.09	0.78 to 1.54	.2800
Age, years*								
< 50	180	11	171	10.0	8.5 to 11.0			
50-59	425	27	401	11.1	10.3 to 12.6	0.89	0.74 to 1.07	
60-69	619	39	585	11.8	11.1 to 12.8	0.83	0.70 to 0.99	
70+	353	22	334	9.5	8.4 to 10.9	0.93	0.77 to 1.12	.1567
Marital status								
Single	101	6	100	9.5	8.1 to 10.7			
Married	1,047	66	977	11.2	10.4 to 12.2	0.81	0.66 to 1.00	
Separated	39	2	38	12.1	8.0 to 14.0	0.94	0.64 to 1.37	
Divorced	225	14	220	10.6	9.7 to 11.6	0.95	0.75 to 1.21	
Widowed	165	10	156	11.7	9.5 to 13.5	0.81	0.62 to 1.04	.1060
PS								
0	609	39	556	14.7	13.6 to 16.1			
1	820	52	789	9.8	9.0 to 10.4	1.47	1.31 to 1.64	
2	148	9	146	6.1	3.9 to 7.5	2.52	2.06 to 3.08	< .0001
Chest pain								
No	1,073	68	1,006	11.8	11.0 to 12.7			
Yes	504	32	485	9.5	8.4 to 10.5	1.27	1.13 to 1.42	< .0001
Dyspnea								
No	802	51	740	12.3	11.3 to 13.3			
Yes	775	49	751	10.0	9.4 to 10.7	1.26	1.14 to 1.40	< .0001
Bone pain								
No	1,325	84	1,244	11.6	10.9 to 12.3			
Yes	252	16	247	7.6	6.7 to 9.2	1.28	1.11 to 1.48	.0006
CNS symptoms								
No	1,513	96	1,431	11.0	10.5 to 11.7			
Yes	64	4	60	8.5	6.0 to 10.9	1.24	0.95 to 1.62	.1123
Duration of symptoms, months								
< 3	1,050	67	993	10.9	10.3 to 11.6			
3-6	361	23	342	10.7	9.0 to 11.8	1.00	0.88 to 1.13	
> 6	166	11	156	11.8	10.3 to 13.9	0.93	0.78 to 1.10	.6938
Weight loss, %								
None to < 5	1,169	74	1,095	12.6	11.7 to 13.5			
≥ 5	408	26	396	7.4	6.5 to 7.8	1.55	1.37 to 1.75	< .0001
Liver metastases								
No	1,353	86	1,271	11.8	11.1 to 12.7			
Yes	224	14	220	6.4	5.8 to 7.4	1.49	1.27 to 1.75	< .0001
Adrenal metastases								
No	1,418	90	1,335	11.5	11.0 to 12.2			
Yes	159	10	156	6.4	5.7 to 7.6	1.29	1.08 to 1.55	.0055
Bone metastases								
No	1,285	81	1,202	12.2	11.4 to 12.9			
Yes	292	19	289	7.4	6.2 to 8.0	1.34	1.16 to 1.54	< .0001
Brain								
No	1,555	99	1,470	11.0	10.5 to 11.6			
Yes	22	1	21	6.5	3.2 to 13.6	1.24	0.78 to 1.98	.3644
WBC ≥ 8.7×10^3								
No	768	49	718	12.2	11.4 to 13.6			
Yes	809	51	773	9.9	9.0 to 10.6	1.20	1.08 to 1.33	.0005

(continued on following page)

Table 2. Characteristics of Patients With Lung Cancer and Survival Rates (continued)

Predictor	No. of Patients	%	No. of Patients Dead	Survival Time (months) Median	95% CI	Hazard Ratio	95% CI	P (χ^2)
Hemoglobin ≥ 14.6 g/dL								
No	1,271	81	1,206	10.4	9.8 to 11.0			
Yes	306	19	285	13.4	12.2 to 14.6	0.80	0.70 to 0.92	.0014
Platelets ≥ 400,000								
No	1,138	72	1,072	12.2	11.5 to 13.3			
Yes	437	28	417	8.5	7.8 to 9.3	1.34	1.19 to 1.51	< .0001
Alkaline phosphatase ≥ 100 U/mL								
No	853	54	798	12.6	11.6 to 13.6			
Yes	721	46	690	9.1	8.5 to 10.2	1.24	1.11 to 1.38	< .0001
Education								
Grades 1-8	206	13	196	11.3	9.7 to 13.9			
Grades 9-11	284	18	273	11.0	9.8 to 12.9	1.04	0.86 to 1.26	
High school graduate	524	33	496	10.5	9.5 to 11.4	1.06	0.90 to 1.26	
Some college	355	23	333	11.3	10.3 to 12.6	0.94	0.78 to 1.12	
College degree	208	13	193	11.1	10.0 to 13.1	1.00	0.81 to 1.23	.5141

Abbreviation: PS, performance status.
*Age at enrollment onto clinical trial.

status (PS) = 1 or PS = 2 (62%). Additional characteristics of this patient population are provided in Table 2.

Table 3 summarizes the relationship between grade school education and other patient characteristics. Specifically, the table shows that patients with less education are more likely to be male, nonwhite, older, had a PS of 1 to 2, or presented with chest pain.

Table 2 also provides information about the relationship of each individual baseline patient characteristic to survival. These analyses show that the following individual factors to be significant predictors of better survival: Female sex, PS = 0, lack of chest pain or dyspnea at diagnosis, low weight loss, lack of liver, adrenal, or bone metastases at diagnosis, WBC less than 8.7×10^3, HGB less than 14.6 g/dL, platelets less than 400,000, and alkaline phosphatase level less than 100 U/mL.

All variables statistically significant at the 0.25 level of significance in univariate analyses presented in Table 2 were considered as candidate variables in a multivariable analysis. Table 4 summarizes the resulting multivariable model that includes the following significant predictors: sex, PS, married, presence of dyspnea,

Table 3. Relationship Between Education and Selected Prognostic Factors

Predictor	Patients With Grade 1-8 Education No.	%	Patients With Grade 9-11 Education No.	%	Patients Who Graduated High School No.	%	Patients With Some College Education No.	%	Patients Who Graduated College No.	%	Total Patients No.	%	P
Sex													.0002
Male	156	15	191	18	326	31	219	21	155	15	1,047	66	
Female	50	9	93	18	198	37	136	26	53	10	530	34	
Race													< .0001
White	151	11	226	17	469	35	304	23	181	14	1,331	84	
Black	29	17	47	28	40	24	38	23	14	8	168	11	
Hispanic	17	43	5	13	9	23	4	10	5	13	40	3	
Other	9	24	6	16	6	16	9	24	8	21	38	2	
Age group, years													.0048
< 50	7	4	35	19	66	37	54	30	18	10	180	11	
50-59	54	13	80	19	144	34	95	22	52	12	425	27	
60-69	83	13	110	18	207	33	136	22	83	13	619	39	
> 69	62	18	59	17	107	30	70	20	55	16	353	22	
Performance status													.0080
0	62	10	106	17	196	32	144	24	101	17	609	39	
1	128	16	144	18	277	34	178	22	93	11	820	52	
2	16	11	34	23	51	34	33	22	14	9	148	9	
Chest pain													.0097
No	123	11	190	18	354	33	248	23	158	15	1,073	68	
Yes	83	16	94	19	170	34	107	21	50	10	504	32	

Table 4. Multivariable Cox Model Predictive of Survival As a Function of Clinical Predictors

Variable	*df*	Parameter Estimate	SE	χ^2	$P(\chi^2)$	Hazard Ratio	95% CI
Female	1	−0.17131	0.06073	7.9579	.0048	0.843	0.748 to 0.949
PS: 1 *v* 0	1	0.28039	0.05973	22.0387	< .0001	1.324	1.177 to 1.488
PS: 2 *v* 0	1	0.66433	0.10804	37.8117	< .0001	1.943	1.572 to 2.401
Married	1	−0.12290	0.05821	4.4578	.0347	0.884	0.789 to 0.991
Dyspnea	1	0.16148	0.05522	8.5526	.0035	1.175	1.055 to 1.310
Weight loss	1	0.18400	0.06575	7.8308	.0051	1.202	1.057 to 1.367
Liver metastases	1	0.27325	0.08402	10.5765	.0011	1.314	1.115 to 1.549
Bone metastases	1	0.30869	0.07287	17.9454	< .0001	1.362	1.180 to 1.571
Hemoglobin ≥ 14.6 g/dL	1	−0.15781	0.07118	4.9157	.0266	0.854	0.743 to 0.982
Platelets ≥ 400,000	1	0.13783	0.06214	4.9196	.0266	1.148	1.016 to 1.296
Adrenal metastases among NSCLC	1	0.36004	0.09861	13.3302	.0003	1.433	1.181 to 1.739
Alkaline phosphatase > 100 U/mL among NSCLC	1	0.17243	0.06385	7.2932	.0069	1.188	1.048 to 1.347
WBC ≥ 8.7×10^3 among extensive/advanced patients	1	0.19829	0.06865	8.3430	.0039	1.219	1.066 to 1.395

Abbreviations: PS, performance status; NSCLC, non–small-cell lung cancer.

weight loss, presence of liver metastases, presence of bone metastases, hemoglobin levels, and platelet levels. Statistically significant interactions were also included in the final model; they showed that the presence of adrenal metastases and levels of alkaline phosphatase levels were important prognostically among patients with NSCLC, and that WBC level was an important predictor among patients with advanced or extensive disease. A residual analysis confirmed the adequacy of the proportional hazards assumption.

The relationship between education and survival without adjustment for known prognostic factors was not statistically significant (Fig 1; Table 2). Two descriptors of low education were added to the multivariable clinical model presented in Table 4 to determine whether low education provided any prognostic information beyond that provided by known prognostic factors. The resulting likelihood ratio test showed that neither an education less than 8 years nor an education less than high school, were significant predictors of poor survival.

DISCUSSION

Statistical analyses reported in this article showed that among lung cancer patients enrolled onto CALGB trials education level was not predictive of survival. Clinical trials are characterized by patient populations that are relatively homogeneous clinically at study entry due to strict eligibility criteria, and by standardized treatment plans. These results substantiated the a priori hypothesis that during "active" protocol treatment and during the lifetime of protocol follow-up among patients with poor prognosis, social conditions as measured by education level do not have an impact on survival. Patients with low education, defined as less than an eighth grade education, enroll onto CALGB clinical studies with poorer prognostic factors, as measured by low ECOG performance status, old age, and presence of chest pain (Table 3). However, after adjustment for the patient's baseline clinical status, education or social condition did not have an impact on survival after clinical trial enrollment, given that all study participants, regardless of education, were carefully and intensively followed until treatment failure and death. Two recent CALGB publications authored by Blackstock[51,52] studied one aspect of the patient's social condition—race—in a population of patients with advanced NSCLC and extensive SCLC, respectively, and found that social conditions which lead to African Americans presenting with poorer prognostic factors, did not have an impact on survival after enrollment onto the clinical trial.

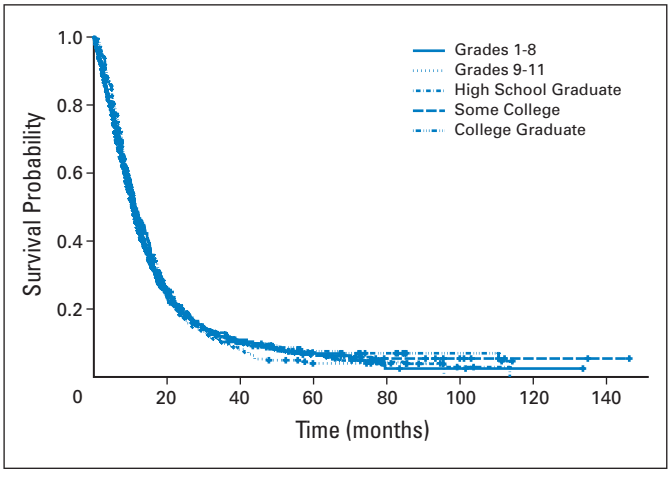

Fig 1. Survival stratified by educational level attained by patient.

Dale[18] has developed the minimal requirements for a well-designed study examining race-cancer mortality issues that is easily adapted to studies examining the relationship between SES and cancer survival: (1) measures of SES should be on the individual level and not be estimated from census data, (2) SES should include at least (individual level) measures of income and education, (3) sample sizes should be adequate for the relevant population to make scientifically and statistically sound inferences, and (4) specific cancer sites should be studied separately.

The criteria adapted from Dale[18] suggest that the study described in this article is well-designed to investigate the relationship between SES and cancer survival in that SES, as measured by education, is available on the individual patient level, the sample size is large enough to assure statistically sound inferences, and a relatively homogeneous population (ie, one cancer site) has been studied. The inclusion of patient-reported income would have strengthened the study; however, such data was purposely not collected as previous pilot work had indicated that a large percentage of patients would not provide such data.[30]

The results reported in this article are not consistent with that reported by Cella et al.[7] In contrast to the relatively homogeneous population considered in this study, Cella considered a heterogeneous cancer patient population that had varying prognoses or expected survival times. Some of Cella's patient population had relatively poor prognoses such as the patients included in the current article; however, others had relatively better prognoses. It is hypothesized that patients who have a prognosis that is much longer than the treatment regimen and the initial period of intensive clinical trial follow-up will ultimately be followed by a period of less intensive monitoring during which a patient's poorer social condition (or education) will negatively influence patient health and survival. The inclusion of these patients with better prognoses in Cella's analyses could have influenced the overall results of his analyses.

The current study did not include patients with early stage NSCLC as such patients were not represented in the database used. A natural question to ask is whether results found in this study would be applicable to such patients if they had participated in CALGB clinical trials. The prognosis of patients with early stage NSCLC is much longer than the treatment regimen and the initial period of intensive clinical trial follow-up. As discussed above, it is hypothesized that patients with such a prognosis will ultimately be in a position where they are not monitored or followed as intensively, and a patient's poorer social condition (or education) will negatively influence patient health and survival. The research of Ou et al[19] and Sowah et al[20] are supportive of this hypothesis in that they found patients with early stage NSCLC who were of low SES to have higher mortality. However, these inferences were based on analyses that involved composite estimates of income derived from census data, and not patient-reported data. In addition, these analyses were also not generated within the context of a clinical trial. Additional research needs to be conducted to assess the relationship between SES/education and survival among patients with early stage NSCLC enrolled onto clinical trials.

The patients studied in this article have all participated in a clinical trial, and may not be completely representative of the greater lung cancer patient population. Hence the study conclusion that education, as a proxy for SES, does not affect the survival of patients with SCLC or stage III/IV NSCLC is limited to participants of clinical trials. Standardization of the treatment in clinical trials insures that all patients are given the same treatment, irrespective of their educational status, as well as probably other SES factors. Additional research is needed to determine if it is appropriate to extrapolate study inferences to patients who do not participate in clinical trials.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

Conception and design: James E. Herndon II, Alice B. Kornblith, Jimmie C. Holland, Electra D. Paskett
Collection and assembly of data: James E. Herndon II
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Appendix

The Appendix is included in the full-text version of this article, available online at www.jco.org. It is not included in the PDF version (via Adobe® Reader®).

