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ORIGINAL REPORT

Analysis of Treatment Practices for Elderly Cancer Patients in Ontario, Canada

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Authors' disclosures of potential conflicts of interest are found at the end of this article.

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ABSTRACT

Purpose
Older patients are underrepresented in many areas of cancer services utilization and in clinical trial enrollment. This study evaluates whether age, when adjusted for sex, comorbidity, stage, tumor site, geography, and time period, is predictive of cancer treatment practice.

Methods
First, we used the Ontario Cancer Registry (OCR) to examine for any apparent differences in treatment practices between elderly (≥ 70 years) and younger patients in the last three decades. Second, we performed a chart review of 1,505 patients with lung, breast, and colorectal cancers seen in Ontario either at an urban center, the Princess Margaret Hospital, or at a rural center, the Northwestern Regional Cancer Centre. Patients were randomly selected from two time periods, 1977 to 1978 and 1997; and the study population was to comprise at least 50% elderly patients.

Results
OCR data demonstrated that, in some settings, such as colorectal cancer, the proportions of elderly cancer patients who were referred to cancer centers and who received any cancer treatment were lower than their younger counterparts. The chart review data showed that increasing age was a significant negative predictor for receiving any cancer treatment ($P < .001$, multivariate analysis) and for having a clinical trial discussion with the treating specialist ($P < .001$, multivariate analysis).

Conclusion
Independent of other factors, older age is consistently a cause of disparity in cancer treatment practice and in clinical trial discussion with patients. By increasing the accrual rate of elderly cancer patients in clinical trials, a better understanding of appropriate therapies for this patient population can be obtained and may, thereby, impact on their cancer-related morbidity and mortality.

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INTRODUCTION

Care of the elderly has become an ever increasingly important field in medicine because the fastest growing segment of the population is composed of individuals 65 years of age or over. Increasing age is also directly associated with increasing rates of cancer, corresponding to an 11-fold greater incidence in persons older than 65 years versus those younger than 65 years.[1] Not only do elderly persons bear a disproportionate burden of cancer, but advancing age also is associated with increased vulnerability to other age-related heath problems.[2] This segment of the population presents a challenge to health care workers, not only because of its growing numbers but also because of the complexity of its health issues.

Aging is a highly individualized, multidimensional process where chronologic age does not always predict the physiologic

decline in an individual because, in part, of the effect of comorbidity.[3] Changes in individual pharmacokinetics, pharmacodynamics, and the tolerance of normal tissues may influence the effectiveness and the safety of cancer treatment in this population.[4] Older individuals with comorbidities are also at risk for functional disabilities, which can impact on cancer treatment strategies. Cancer treatment decision making requires a multidisciplinary and multidimensional assessment of both the characteristics of the malignant disease and the patient's general health status.[5]

To provide evidence-based literature on the evaluation and management of elderly patients with cancer, clinical trials are needed to guide medical professionals in their decisions. Even though, in 1989, the Food and Drug Administration issued a recommendation that elderly patients should not be excluded from clinical trials,[6] the underrepresentation of elderly patients in cancer treatment trials is a persistent problem.[7-12] Without well-designed clinical trials that include sufficient numbers of elderly cancer patients, it becomes difficult to determine how this population should be treated. This age-dependent discrepancy is not unique to clinical trial participation; it also exists in the prescription of routine health care. Whether it is a result of the lack of evidence-based information about elderly patients with cancer or a result of a widespread opinion that geriatric patients do not tolerate cancer therapies well, it remains apparent that elderly patients are not using standard cancer services as much as their younger counterparts.[13-18]

Although one might assume that the decreased rate of clinical trial accrual and reduced cancer services utilization by elderly patients might be a result of their poor functional status and resultant inability to tolerate cancer therapies, this is not clearly the case. Many studies have attempted to evaluate whether elderly patients suffer from more toxicity than their younger counterparts, therefore justifying an approach of less-aggressive care in this population. The research in this field still remains contradictory. Several trials have shown an increased risk of toxicity or a need for stem-cell support for myelosuppression in the elderly,[19-24] whereas other studies have shown an almost equivalent toxicity profile between older and younger patients.[25-30]

Given the exponential growth of the elderly population, the increasing prevalence of cancer with age, and the need to improve the health status and quality of life of the elderly, it is important to identify the barriers to access of cancer management to reduce the disparity in the care of elderly cancer patients. The first step in optimizing the treatment of elderly patients with cancer is to determine whether age is a cause of disparity in treatment and accrual onto clinical trials. To this end, we have performed a retrospective review to assess the influence of age and other factors, such as comorbidity, geographic location, stage, and type of cancer, on standard treatment delivery and clinical trial discussion. If age is in fact a cause of disparity, strategies to overcome this challenge can be planned. Interventions, such as continuing education to oncologists regarding the management of elderly cancer patients and clinical trials developed specifically for geriatric patients, may provide health professionals with a better understanding of appropriate therapies for this patient population and, thereby, ultimately impact on their cancer morbidity and mortality.

METHODS

Canadian Health Care System and Regional Cancer Centers

The Canadian health care system is a publicly financed system that provides universal health care coverage to all eligible Canadian residents. All eligible Canadian residents have reasonable access to medically necessary insured services on a prepaid basis, without direct charges at the point of service. For cancer care delivery in Ontario, there are 10 regional cancer centers (also termed integrated cancer programs) throughout the province to improve access to cancer services in all areas. The Princess Margaret Hospital (PMH) and the Northwestern Regional Cancer Centre (NWORCC) are two such integrated cancer programs. Cancer care services are also available in community hospitals throughout Ontario. Radiation treatments are only available in the regional cancer centers, whereas chemotherapy and surgery are available in the regional cancer centers and in community hospitals.

Part 1: Ontario Cancer Registry

The Ontario Cancer Registry (OCR) is a province-wide database that captures selected information on all patients in Ontario who were diagnosed with cancer as identified through pathology reports. The data collected include demographics, such as sex and date of birth, as well as information regarding where treatments were delivered and what types of treatment were received. The treatment data on patients treated at regional cancer centers (or integrated cancer programs) are more readily accessible in the registry than the data for patients treated only in the community. The OCR does not include information about stage of disease, comorbidity, intent of treatment, or participation in clinical trials.

The OCR database was used to identify any apparent trends and differences in referral patterns and treatment practices between patients $\geq$ 70 years and younger patients in the past three decades for three common cancer sites (lung, breast, and colorectal). The rationale for selecting 70 years as the definition of elderly is based on previous surveys of primary care practitioners and oncologists by our group, in which this chronologic age was considered by the majority of respondents as being the most appropriate in defining elderly.[8,31] Age-stratified plots of patient referrals to cancer centers and of treatment practice patterns, including surgery, radiotherapy, and chemotherapy, were constructed based on OCR data from 1965 to 1998. Formal statistical analyses of these plots were not undertaken, but obvious differences observed based on age provided support for further evaluation. Because it was not possible to ascertain whether the differences demonstrated in referral rates and treatment practices were confounded by other factors, such as cancer stage and comorbidity, an in-depth review of health records from two geographically distinct Ontario cancer centers over two separate time points was performed.

Part 2: Retrospective Chart Review

Study sample population. The sample population included all patients over the age of 35 years with lung, breast, or colorectal cancer who were referred for the first time to either PMH or NWORCC over two different decades (1977 to 1978 or 1997). These cancer types were selected because they were common cancers and had shown a difference in referral and treatment rates between the older and younger age groups in the OCR data. The two geographically distinct Ontario cancer centers were chosen to obtain treatment practice information representative of an urban center (PMH) and a rural center (NWORCC). The years 1977 to 1978 and 1997 were chosen to determine whether treatment practices for elderly cancer patients had evolved over time.

Study design. A retrospective chart review of random samples of patients who met the study sample population criteria was performed. To identify relevant charts at PMH, the hospital cancer registry database was used, which captures basic demographic information on all patients diagnosed with cancer and seen at PMH. Using the PMH registry, the total numbers of patients with lung, breast, and colorectal cancer who were classified as less than 70 or $\geq$ 70 years of age and were referred for the first time to PMH in 1977, 1978, or 1997 were obtained. Computer-generated numbers were then used to select charts randomly. The number of random charts reviewed represented 10% (237 of 2,404 patients) and 21% (597 of 2,826 patients) of the total number of patients seen for the first time at PMH in 1977 to 1978 and 1997, respectively. Approximately one third of the charts reviewed were chosen from 1977 to 1978, and two thirds were chosen from 1997 because more recent treatment practice patterns were felt to provide information of greater relevance and interests. A similar approach was taken to identify relevant charts at NWORCC. Because of the smaller numbers of new patients seen each year at NWORCC compared with PMH, all patients who met the study sample population criteria were included from NWORCC for the two time periods.

The charts were reviewed to identify relevant information, including purpose of visit (eg, consultation *v* second opinion), geographic distance between home residence address and the cancer center, tumor stage, comorbidity as evaluated by the Charlson score, type(s) of treatment received (eg, chemotherapy, surgery, or radiotherapy), intention of treatment (eg, curative or palliative), discussion about clinical trial participation, entry onto clinical trial, and reason for not enrolling onto a clinical trial if discussed.

Study analysis. Comorbidity was measured using the Charlson score, which was calculated based on data extracted from charts. This parameter was analyzed univariately in two different ways (comparisons between Charlson scores of $\leq$ 1 *v* $\geq$ 2, or comparisons between Charlson scores of 0, 1, or $\geq$ 2). For multivariate analyses involving comorbidity, the former definition was used for the primary analysis to coincide with common practice found in the literature. If pathology data were available, pathologic tumor-node-metastasis (TNM) status was used to determine the tumor stage because this is the most accurate form of cancer staging. When pathologic information was unavailable, clinical TNM status was then used. Palliative stage was defined in colorectal or breast cancer patients with M = 1 status (regardless of T or N status) and in lung cancer patients with T = 4, N = 3, or M = 1 staging statuses. All other patients with known TNM staging were classified as curative in stage.[32]

Distance to cancer center was calculated as linear distance from the patients' listed residence to the cancer center in which they were treated (PMH or NWORCC) via the forward sorting area (FSA). The FSA is denoted by the first three alpha-numeric digits in the Canadian postal code. The midpoint for each FSA was obtained by using the postal code conversion file,[33] which was obtained from the data library service of the University of Toronto, Toronto, Ontario, Canada. Each patient (and each cancer center) was assumed to reside at this central point of their respective FSA. The distance between the patients' residence FSA midpoint and the hospital FSA midpoint was calculated using the following formula: Distance = $6370.997 \times \arccos[\sin(\text{lat\_r}) \times \sin(\text{lat\_h}) + \cos(\text{lat\_r}) \times \cos(\text{lat\_h}) \times \cos(\text{long\_r–long\_h})]$; where lat_r is latitude/57.29577951 of the patients' residence, long_r is the longitude/57.29577951 of the patients' residence, lat_h is latitude/57.29577951 of the hospital location, and long_h is the longitude/57.29577951 of the hospital location.

This formula assumes that the earth is a perfect sphere with a radius of 6370.997 km and that patients will live randomly throughout a given FSA. Thus, the midpoint represents an unbiased estimate of the true location for all patients. Patients living in the same FSA as PMH were assigned a residence distance of 0.25 km from PMH, and those living in the same FSA as NWORCC were assigned a residence distance of 1.5 km from NWORCC (these distances are approximately one third of the distance of the width of the respective FSA). Transformation of the distance to the log scale was performed to normalize the data.

Statistics. Summary statistics, such as the mean, standard deviation, proportion, and interquartile range, were used to describe the patient population. Patients were grouped based on their age ($<$ 70 or $\geq$ 70 years) on the date they were first seen at either NWORCC or PMH. To reduce the effect of multiple testing, selected variables were chosen a priori and tested as potential predictors of whether a patient received treatment (any surgery, radiotherapy, or chemotherapy) and whether a patient was involved in a discussion of potential enrollment onto a clinical trial using univariate logistic regression.

Variables selected as potential predictors were sex, age, comorbidity assessed using the Charlson score, primary site of cancer, year of treatment, cancer center, distance from cancer center, and stage of cancer. Multivariate analyses were conducted by constructing a model containing all of these variables and testing whether age was statistically significant after adjusting for all other variables in the model. For the primary multivariate analyses, sex was excluded because of the high colinearity with primary cancer site (ie, breast cancer patients were all female), and distance was excluded because of large numbers of missing data ($\geq$ 13% of all patients) and nonsignificant univariate results.

The analysis was repeated including sex, distance, and age as a continuous variable and with a different categorization of the Charlson score (ie, three groups: 0, 1, and $\geq$ 2). With age as a continuous variable, the odds ratio is reported for 10-year increments for ease of interpretation because the level of statistical significance is not influenced by the choice of increment intervals. Breast cancer patients were excluded from subsequent analysis of whether the patient received any treatment because investigators were unable to reliably determine whether hormonal treatment was received. Prescription records of hormonal therapy were not always identifiable in the charts, and there was no way of ascertaining patient compliance.

Bootstrapping of the results of the logistic regression analyses was performed as a check of the results in case of nonnormality.[37] Five hundred bootstrap replications of the data were formed for

each analysis using S-plus (Version 3.3; Statistical Sciences, Seattle, WA) 2000 (MathSoft, Inc., Cambridge, MA), and logistic regression was performed on each sample. Univariately, the percentage of bootstrap samples for which the univariate variable was significant was recorded. Multivariately, a forward stepwise selection procedure was used, and the percentage of bootstrap samples in which a variable entered the model was calculated. Ideally, one would have many samples of data, and the results for each sample would be tested separately. This repeated sampling could then demonstrate whether the single result observed was significant (or nonsignificant) as a result of chance or as a result of a few outlier data points in the original sample or was a true result. By bootstrapping, one artificially creates multiple samples of the data, and tests are performed on each sample. Thus, if a given variable is significant in the majority of bootstrap samples, this would indicate that a small *P* value is more likely because of a true association. Conversely, if a given variable is significant in only a few bootstrap samples, this indicates that a small *P* value may be a result of chance or of some outliers.

It was also of interest to investigate whether there was an association between age and initial visit at PMH or NWORCC. As a surrogate for this association, the mean distance from the cancer center was computed for patients less than 70 and ≥ 70 years old and compared using a two-sample *t* test.

Data accuracy. Charts at PMH were reviewed by four abstractors (C.T., K.N., and two research coordinators); charts at NWORCC were reviewed by two abstractors (B.P. and J.K.). A random sample of 10% of the charts was cross audited for each of the abstractors for data quality purposes. The overall error rate was estimated to be 1.35%.

Institutional review board approval. The conduct of this study was approved by the Institutional Review Boards of University Health Network and NWORCC.

RESULTS

Part 1: Ontario Cancer Registry

OCR data demonstrated that with some cancers, such as colorectal cancer, the proportions of elderly cancer patients who were referred to cancer centers and subsequently received any cancer treatment were lower than for their younger counterparts. Figure 1A and 1B are sample age-stratified plots of referral and treatment rates for colorectal cancer, and similar plots exist for breast and lung cancers. Formal statistical analyses of these plots were not undertaken, but these findings prompted further investigations into the exact treatment practices for elderly cancer patients when they were seen at cancer centers.

Part 2: Retrospective Chart Review

There were 1,505 patients (868 from PMH and 637 from NWORCC) who had their charts reviewed for this study. Twenty-six patients who were less than 35 years old at the time of first consult at PMH or NWORCC and 19 patients whose first date of consult was not in 1977, 1978, or 1997 were excluded from the database. Descriptive statistics for the 1,460 patients included in the final data set, as grouped by age (< 70 *v* ≥ 70 years), are listed in Table 1. There are no significant differences in demographic characteristics between those patients less than 70 or ≥ 70 years of age.

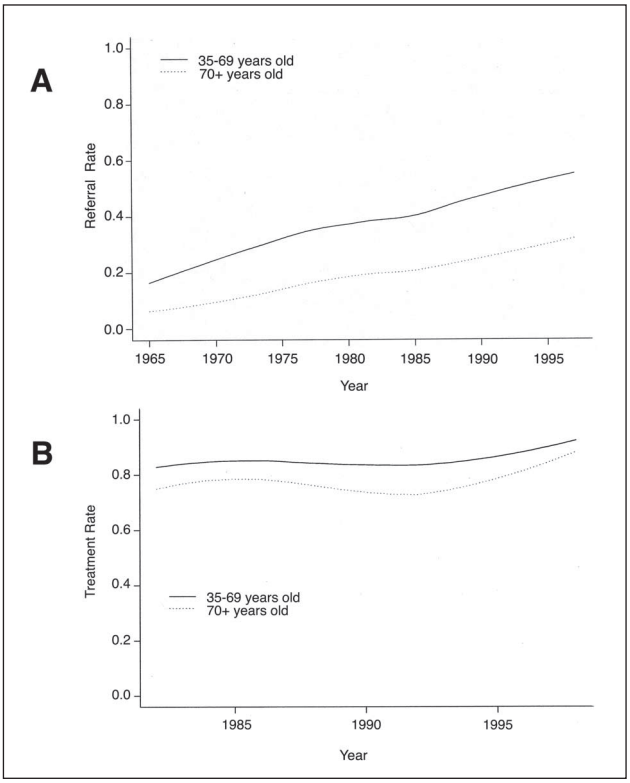

Fig 1. (A) Age-stratified plots of referral rates for colorectal cancer patients in Ontario, Canada, between 1965 and 1998. Data were obtained from the Ontario Cancer Registry. (B) Age-stratified plots of rates of any cancer treatment (including surgery, radiation, or chemotherapy) for colorectal cancer patients in Ontario, Canada. Data are obtained from the Ontario Cancer Registry.

Predictors of receiving any cancer treatment. Table 2 provides the univariate logistic regression analyses of potential predictors of whether patients received any cancer treatment, including chemotherapy, radiation therapy, and/or surgery. Age, when analyzed either as a binary (< 70 *v* ≥ 70 years) or as a continuous variable, was significantly associated with whether the patient received treatment. After adjusting for all other variables, including comorbidity, primary site of cancer, year of treatment, cancer center, and stage of cancer, age remained highly significant in the multivariable model ($P < .001$; Table 3). The odds of a patient 70 years of age or older receiving any cancer treatment was 50% of that of a patient under age 70 years, after adjusting for other variables in the model. Thus, age is associated with whether or not a patient will receive cancer treatment once he or she is referred and seen at a cancer center, regardless of other factors such as tumor stage or comorbidity.

Age remained a significant predictor for receipt of any cancer treatment in secondary analyses when additional variables, including sex, distance, and a different categorization of the Charlson score (ie, three groups: 0, 1, and ≥ 2),

Table 1. Descriptive Statistics of All Patients Grouped by Age

Statistic	All Patients (N = 1,460)		< 70 Years Old (n = 761)		≥ 70 Years Old (n = 699)	
	No.	%	No.	%	No.	%
From an urban cancer center, PMH	834	57.1	387	50.9	447	64.0
Female	910	62.3	510	67.0	400	57.2
Primary site						
Breast	592	40.6	355	46.7	237	33.9
Colorectal	397	27.2	182	23.9	215	30.8
Lung	471	32.3	224	29.4	247	35.3
Purpose of visit						
Consultation	1,397	95.7	725	95.3	672	96.1
Second opinion only	63	4.3	36	4.7	27	3.9
Year of consult						
1977/1978	486	33.3	258	33.9	228	32.6
1997	974	66.7	503	66.1	471	67.4
Stage						
Curative	870	59.6	484	63.6	386	55.2
Palliative/metastatic	443	30.3	222	29.2	221	31.6
Unknown	147	10.1	55	7.2	92	13.2
Charlson score						
0	816	55.9	491	64.5	325	46.5
1	281	19.3	122	16.0	159	22.8
2	156	10.7	56	7.4	100	14.3
3	56	3.8	15	2.0	41	5.9
4	22	1.5	11	1.5	11	1.6
5+	129	8.8	66	8.7	63	9.0
Treated, any treatment	1,338	91.6	722	94.9	616	88.1
Surgery intent						
Curative	611	41.9	386	50.7	225	32.2
Palliative	58	4.0	22	2.9	36	5.2
Given but intent unknown	169	11.6	96	12.6	73	10.4
No surgery	622	42.6	257	33.8	365	52.2
Radiotherapy intent						
Curative	458	31.4	300	39.4	158	22.6
Palliative	457	31.3	189	24.8	268	38.3
Given but intent unknown	61	4.2	46	6.0	15	2.2
No radiotherapy	484	33.2	226	29.7	258	36.9
Chemotherapy intent						
Curative	254	17.4	180	23.7	74	10.6
Palliative	181	12.4	123	16.2	58	8.3
Given but intent unknown	63	4.3	43	5.7	20	2.9
No chemotherapy	962	65.9	415	54.5	547	78.3
Discussed CT	221	15.1	147	19.3	74	10.6
Enrolled onto CT/No. of patients who discussed a CT	115/221	52.0	81/147	55.1	34/74	46.0
Reasons for not enrolling						
Ineligible	29	27.4	19	28.8	10	25.0
Logistical	1	0.9	1	1.5	0	0.0
No suitable trials available	3	2.8	1	1.5	2	5.0
Patient/family decision	56	52.8	32	48.5	24	60.0
Physician decision	6	5.7	5	7.6	1	2.5
Other/not mentioned	11	10.4	8	12.1	3	7.5
Age at first consult, years						
Mean	67.5		57.3		78.5	
SD	13.0		8.7		6.0	
Age at pathology, years						
Mean	66.3		56.6		77.4	
SD	13.1		9.0		6.6	
Kilometers from cancer center						
Median	11.1		13.4		10.0	
IQR	6.1-86.1		6.3-93.7		5.8-77.9	

Abbreviations: PMH, Princess Margaret Hospital; CT, clinical trial; SD, standard deviation; IQR, interquartile range.

Table 2. Univariate Predictors of Receiving Any Treatment

Variable	Odds Ratio	95% CI	*P*	Bootstrap % Significant
Sex, female*	1.07	0.68 to 1.67	.78	72
Age†	0.63	0.53 to 0.74	< .001	100
≥ 70 *v* < 70 years old	0.40	0.27 to 0.60	< .001	100
Charlson score, *v* 0				
1	0.56	0.34 to 0.90	.016	64
2	0.46	0.30 to 0.71	< .001	17
Charlson score, 2+ *v* 0-1	0.55	0.38 to 0.82	.003	83
Primary site, *v* lung				
Breast	2.63	1.66 to 4.16	< .001	56
Colorectal	1.50	0.96 to 2.34	.075	93
Year, 1997	1.02	0.69 to 1.50	.94	5
Hospital, rural	1.60	1.08 to 2.37	.02	68
Stage, *v* palliative				
Curative	3.77	2.46 to 5.78	< .001	100
Missing	0.83	0.50 to 1.39	.49	88
Distance	0.99	0.87 to 1.13	.89	9

*Breast cancer patients excluded.
†In 10-year increments.

were entered into the multivariable model. However, when all breast cancer patients were excluded from the analysis because it was impossible to reliably determine whether hormonal treatment was received by patients, age only approached statistical significance ($P = .067$ as a continuous variable and $P = .12$ as a binary predictor). This result should be interpreted cautiously because only a small number of patients did not receive any treatment, regardless of primary cancer site. For instance, only 92 patients with colorectal or lung cancer did not receive treatment, and of these, only 34 were less than 70 years old.

Besides age, other factors that also significantly predicted for patients receiving any cancer treatment in a multivariate analysis included having breast cancer as a primary site, being seen at a rural cancer center, and having curative stage disease (Table 3). Comorbidity was of borderline significance, whereas the year of being first seen at a cancer center was not a significant predictor.

Table 3. Multivariate Predictors of Receiving Any Treatment

Variable	Odds Ratio	95% CI	*P*	Bootstrap % Significant
≥ 70 *v* < 70 years old*	0.50	0.33 to 0.76	< .001	97
Charlson score, 2+ *v* 0-1	0.68	0.45 to 1.03	.07	58
Primary site, *v* lung				
Breast	1.73	1.06 to 2.82	.029	63
Colorectal	1.52	0.95 to 2.43	.08	54
Year, 1997	1.03	0.69 to 1.56	.85	23
Hospital, rural	1.72	1.13 to 2.62	.012	82
Stage, *v* palliative				
Curative	3.12	1.98 to 4.90	< .001	100
Missing	0.72	0.42 to 1.24	.24	49

*Note, age reached statistical significance after adjusting for other variables, regardless of whether age was defined as a binary variable (< 70 *v* ≥ 70 years) or defined as a continuous variable ($P < .001$).

Predictors of clinical trial discussion. Table 4 lists the results of the univariate logistic regression analyses of potential predictors for whether a clinical trial was discussed with the patient. Age was significantly associated with clinical trial discussion when analyzed either as a binary (< 70 *v* ≥ 70 years) or as a continuous variable. Age was also significant in almost all (100% and 99%) bootstrap samples. After adjusting for all other variables, including comorbidity, primary site of cancer, year of treatment, cancer center, and stage of cancer, age remained highly significant and entered all multivariate models, as in Table 5. The odds of a patient 70 years or older having a clinical trial discussion was just less than half (48%) that of a patient under 70 years of age, after adjusting for other variables in the model. Age remained statistically significant as a predictor in all secondary analyses, when additional variables including sex, distance, and a different categorization of the Charlson score (ie, three groups: 0, 1, and ≥ 2) were entered into the multivariable model.

Besides age, other factors that also significantly predicted for patients having a clinical trial discussion in a multivariate analysis included having breast cancer as a primary site, being seen at an urban cancer center, and being seen in 1997 as opposed to 1977 or 1978 (Table 5). Comorbidity and tumor stage were not significant predictors for clinical trial discussion. Results were similar when patients who did not receive any treatment (n = 122), for whatever reasons, were excluded. This analysis attempts to adjust for the potential bias associated with patients who

Table 4. Univariate Predictors of Clinical Trial Discussion

Variable	Odds Ratio	95% CI	*P*	Bootstrap % Significant
Sex, female*	1.28	0.82 to 1.98	.28	23
Age†	0.79	0.71 to 0.88	< .001	99
≥ 70 *v* < 70 years old	0.50	0.37 to 0.67	< .001	100
Charlson score, *v* 0				
1	0.62	0.41 to 0.93	.021	70
2	0.64	0.45 to 0.93	.017	91
Comorbidity, 2+ *v* 0-1	0.72	0.50 to 1.02	.065	46
Primary site, *v* lung				
Breast	2.25	1.59 to 3.18	< .001	100
Colorectal	0.90	0.58 to 1.40	.65	49
Year, 1997	9.87	5.57 to 17.49	< .001	100
Hospital, rural	0.41	0.30 to 0.56	< .001	100
Stage, *v* palliative				
Curative	1.56	1.11 to 2.18	.010	100
Missing	0.90	0.50 to 1.63	.72	49
Distance	0.97	0.89 to 1.06	.55	4

*Breast patients excluded.
†In 10-year increments.

Table 5. Multivariate Predictors of Clinical Trial Discussion

Variable	Odds Ratio	95% CI	*P*	Bootstrap % Significant
≥ 70 *v* < 70 years old*	0.48	0.34 to 0.66	< .001	100
Comorbidity, 2+ *v* 0-1	0.95	0.64 to 1.40	.78	14
Primary site, *v* lung				
Breast	1.86	1.24 to 2.77	.003	98
Colorectal	0.83	0.53 to 1.32	.44	22
Year, 1997	9.11	5.11 to 16.25	< .001	100
Hospital, rural	0.44	0.31 to 0.62	< .001	100
Stage, *v* palliative				
Curative	0.98	0.66 to 1.45	.90	13
Missing	1.08	0.56 to 2.05	.82	12

*Note, age reached statistical significance after adjusting for other variables, regardless of whether age was defined as a binary variable (< 70 *v* ≥ 70 years; $P < .001$) or defined as a continuous variable ($P = .006$).

might have chosen not to receive any treatment or who were never offered any treatment and, thus, who may not have been engaged in any discussion involving clinical trial participation.

Distance

On average, patients who were ≥ 70 years old lived closer to the cancer center than those less than 70 years old (on log scale of 2.64 *v* 2.85 log [km], respectively; $P = .02$). When analyzed separately for each of the two cancer centers, this association was significant for patients who went to PMH (log scale of 2.65 *v* 2.95 log for ≥ 70 and < 70 years of age, respectively; $P = .002$) but not for NWORCC patients (log scale of 2.49 *v* 2.65 log for ≥ 70 and < 70 years of age, respectively; $P = .43$). One possible explanation for the lack of significant association seen among NWORCC patients is the lack of variability in the estimated distance between patients. In the rural areas, FSAs are larger, and a higher percentage of patients came from the same FSA. As distance was measured from the center of a patient's residential FSA to the cancer center's FSA, this resulted in less variability (for example, 79% of NWORCC patients with residential address known came from only five FSAs, whereas no more than 3% of PMH patients resided in the same FSA).

DISCUSSION

This study demonstrated that the proportion of elderly cancer patients referred to cancer centers and who subsequently received any cancer treatment has consistently been lower than their younger counterparts. The two cancer centers selected, PMH and NWORCC, are representative of typical urban and rural centers in Ontario, respectively. An in-depth chart review showed that increasing age was a significant ($P < .001$, multivariate analysis) negative predictor for receipt of any cancer treatment. In addition, increasing age was a negative predictor of patients having a clinical trial discussion with their cancer specialists ($P < .001$, multivariate analysis). These results were consistent over two decades, when cancer care has been evolving and improving with better interventions available for the management of treatment-induced side effects. These findings suggest that, despite factoring in potential confounders such as tumor stage and comorbidity, chronologic age alone is associated with a significant disparity in the delivery of standard therapy or participation in clinical trials. Furthermore, given that the Canadian health care system provides universal care to all, the lack of financial barrier did not seem to minimize this age-dependent discrepancy.

Besides age, other factors that significantly predicted for patients receiving any cancer treatment in a multivariate analysis included being seen at a rural cancer center and having curative stage disease. The additional factors besides age that significantly predicted for patients having a clinical trial discussion in a multivariate analysis included being seen at an urban cancer center and being seen in 1997 as opposed to 1977 or 1978. These results seem logical because one would expect that many patients seen in an urban cancer center were there to seek second opinions and would subsequently return to their referring center for therapy closer to home. The majority of patients seen in a rural cancer center would be local residents, with the intention of the visits being primary consultation and initiation of therapy. Patients with curative rather than palliative stage disease were more likely to undergo cancer treatments. This finding seems plausible because an aggressive approach to achieve cancer cures would be justifiable, regardless of other factors. Last, a larger number of clinical trials would be available in an urban center compared with a rural center and in 1997 compared with two decades earlier. These findings would suggest that the results of our study appear internally valid.

Although this study involved an extensive retrospective chart review and demonstrated the important factor of age in cancer care delivery and clinical trial activity, there are several limitations to our results. Given the retrospective nature of the study, it is possible that other confounding factors that might have influenced cancer care delivery and clinical trial discussion were missed or were poorly documented in medical records. For example, treatments, such as hormonal therapy for breast cancer patients, were not examined in this study because of difficulties in ascertaining prescription records and patient compliance. This caveat could potentially result in an underestimation of the number of patients receiving cancer treatment in this tumor type. However, in our study, breast cancers patients were actually the most likely to receive any cancer treatment compared with the other tumor types. Furthermore, the analysis for clinical trial discussion and enrollment is dependent on clinical trial availability at the specified time periods and for different tumor types. The variability of

clinical trial availability by time and by tumor types might fluctuate just by chance and affect our results. For instance, it is likely that there were more clinical trials available for breast cancer than for colorectal or lung cancer, as reflected by our finding.

Because this study was a retrospective chart review, it cannot reliably determine how patients' preferences may have impacted on treatment decisions. The wishes of patients and their family to accept or decline any treatment offered is obviously of paramount importance when making the final management decision. The treatment choices patients make are also likely to change over the course of their lives. Older patients may be more reluctant to receive treatment if they feel that the risks associated with side effects outweigh the potential time or benefit gained at this stage in their lives. Furthermore, treatment decisions among younger patients may be impacted by career and family obligations, whereas these factors may no longer be as important for older patients. To accurately determine the perspectives and attitudes of older cancer patients contemplating treatment, primary and prospective research evaluating these variables needs to be undertaken.

Although our study used data from a Canadian province, the results can likely be extrapolated to many other countries including the United States. As of September 2000, health care costs of clinical trial participants have been uniformly covered by Medicare in the United States.[38] Thus, cancer patients in the United States should no longer be denied access to clinical trials based on financial reasons. In addition, because cancer treatments frequently involve multiple modalities, including surgery, radiation, and/or chemotherapy, most patients receive their treatment at cancer centers that provide access to all or most of these services. This type of practice set-up is similar to the Canadian system that we have analyzed in our study.

Our finding of age as a cause of disparity in the delivery of standard cancer treatments is concordant with reports from the literature. A Belgian study by Berghmans et al[34] analyzed a database consisting of treatments received by patients with non–small-cell lung cancer. They found that seven (19%) of 60 patients who were 75 years of age or older did not receive the standard treatment based solely on their age, whereas 23 (38%) of 60 patients were excluded from standard treatment based on poor performance status or comorbid illness. Two other studies have examined the undertreatment of older men with prostate cancer.[35,36] They found that age was an independent negative predictor of optimal treatment even when taking into account patients' comorbidities and the stage of their disease. These results are consistent with those found in our study, which further point to the lack of good information about how to treat this patient population.

Part of the reason for the discrepancy in the way older patients are managed compared with their younger counterparts is the lack of any clear consensus on how best to evaluate and treat elderly patients with cancer. In fact, the definition of elderly remains debatable and has evolved with time as medical advances have prolonged life. Seventy years is often considered as the lower limit of senescence because most comorbidity and other age-associated conditions, such as depression and decrease in physical functions, occur for most people at this age.[39] On the basis of this fact as well as the responses to previous surveys of primary care practitioners and oncologists by our group, we chose 70 years as the definition of elderly in this study, although many previous reports have used 65 years in their definitions.[7,8,10-12]

Although many methods and schemes are available to predict the ability of elderly patients to tolerate and benefit from cancer treatment, there is not one established and uniform approach. Methods, such as geriatric assessment,[40] performance status scale,[41] functional status,[42] and toxicity index,[43] have all been proposed as potential evaluation tools to aid oncologists in deciding how to treat elderly cancer patients. Although they all possess different strengths and weaknesses, there is not one tool that has been well validated in this population or that is in widespread use.

Without validated tools and adequate education to make evidence-based decisions, it seems that clinicians continue to be cautious in their approach towards managing elderly patients with cancer. To optimize the treatment of the elderly, clinical trials need to be performed using and validating the various evaluation tools. Clinical trials that either accrue elderly patients in relevant proportions or are designed to accrue specifically elderly patients are necessary so that clinicians can gain experience and comfort in enrolling these patients. Only by obtaining the information from properly conducted clinical trials about the best ways to treat elderly patients with cancer will we be able to optimize their management in the clinical setting. By learning which older patients under what circumstances can tolerate aggressive cancer therapies and which patients need to be treated more conservatively, clinicians will be less fearful of embarking on different therapeutic strategies with their elderly patients. This will hopefully lead to appropriate cancer management in all patients, regardless of their age.

From our findings, both the delivery of cancer treatments and the discussion of clinical trials occurred less frequently among older patients. The decision to withhold standard cancer treatments might be oncologist driven, patient driven, or based on a mutual agreement between both parties. For the discussion of clinical trials, it would seem more likely that oncologists, either intentionally or subconsciously, avoided clinical trial participation as a potential option for older patients. Older patients would unlikely be inquiring about trial options on a voluntary basis. Hence, education for both oncologists and the older patients about standard treatment options and clinical trial opportunities would be equally important in empowering

oncologists and older patients to make appropriate therapeutic decisions.

In conclusion, it seems that, independent of other factors, older age is consistently a cause of disparity in cancer treatment practice and in clinical trial discussion with patients. Elderly patients with cancer are vulnerable to being inappropriately managed because of continuing uncertainties about the feasibility of delivering standard treatments and their tolerability of toxic side effects. By increasing the accrual rate of elderly cancer patients in clinical trials, a better understanding of appropriate therapies for this patient population can be obtained and may ultimately impact on their cancer-related morbidity and mortality.

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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