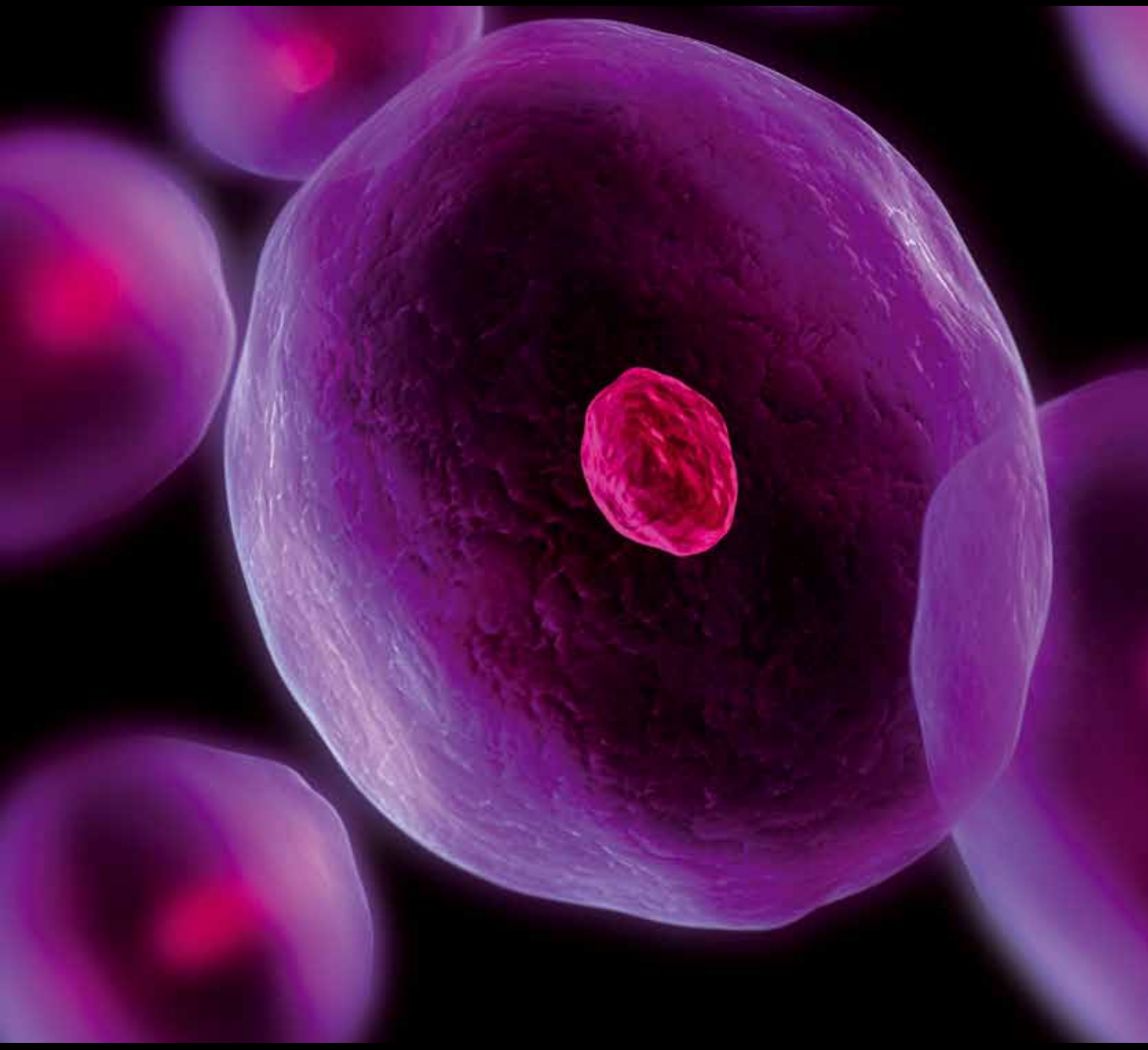
Journal of Cancer Epidemiology

Cancer in the Elderly

Guest Editors: Frank Buntinx, Christine Campbell, and Marjan van den Akker



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Editorial Board

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Editorial

Cancer in the Elderly

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The incidence of cancer rises among older populations [1, 2], and continuous improvement in treatment outcomes is resulting in even greater increases in the prevalence of cancer survivors in this age group [3]. There is considerable variation in cancer mortality rates in the elderly among high-income countries, with the UK having poorer outcomes compared to the USA and Western and Northern European countries [4]. The diagnosis of cancer and treatment decisions following diagnosis at an older age bring specific challenges to health care providers. Further, living with cancer has specific characteristics and consequences for older people. The five papers (three from North America, two from Europe) included in this special issue address some of these topics: increasing awareness of breast cancer symptoms, management of patients with lung and breast cancers, and survivorship issues specific to older patients.

There is good evidence that age is a risk factor for the delay in presentation with breast cancer [5]. L. J. L. Forbes et al. describe the implementation into routine clinical practice of an evidence-based brief intervention designed to promote earlier symptomatic presentation of breast cancer among older women. The authors have previously reported on the effectiveness of the intervention in a randomised control trial [6]; this further work shows that its introduction into routine mammography appointments at four pilot areas within the UK's Breast Screening Programme results in similar levels of breast cancer awareness among participating women (mean age 71 years, 4 months) as in the trial setting. The intervention was acceptable to women and to mammography providers. Given the low awareness of age-related cancer risk within the UK compared to a number of other countries [7], interventions of this nature, conveying key cancer messages as patients are entering the age group with highest risk of breast cancer, have the potential to contribute to earlier health seeking.

Subsequent to a cancer diagnosis, treatment decisions for older patients are often complicated by factors such as frailty, and the presence of comorbidities. M. K. Malik et al. have examined the impact of treatment decisions among women aged 71 and over with a breast cancer diagnosis compared to younger women using a retrospective observational study design in a population of patients receiving potentially curable surgery. Patients were from two health care facilities in NY, USA. The results include differing pathologies between younger and older women and significant differences in proportion of patients given adjuvant or neoadjuvant chemotherapy and radiation therapy. However, among this patient group, undertreatment (defined as lack of adherence to conventional treatment guidelines) did not lead to poorer local or distant disease-free survival compared to appropriately treated individuals. Given the selected population in this study, the authors emphasise the need for optimal treatment regimens to be determined on a case-by-case basis.

Despite legitimate concerns about the ability of some older patients to tolerate aggressive treatments, S. Fisher et al. demonstrate that there are elderly patients who do receive a survival benefit from chemotherapy for small cell lung cancer (SCLC), even at reduced doses. They assessed the uptake and tolerance of chemotherapy among patients aged 75 and older with SCLC in AB, Canada. 68% of patients who were recommended chemotherapy by an oncologist began treatment: 52% completed all cycles, with 41% receiving

reduced chemotherapy doses. Kaplan-Maier survival curves show that patients who completed chemotherapy had a significantly better survival than those who did not, and Cox adjusted hazard ratios show this benefit existed even when the chemotherapy dose was reduced. The authors suggest that elderly patients are at least considered for established treatments, with further research needed into the relationship between frailty and toxicity to help determine who might benefit from chemotherapy treatment.

With an increasing number of cancer diagnoses and improved outcomes, the number of older cancer survivors is increasing. Patients (and their health care providers) must manage not only the sequelae of treatment but also the increasing burden of morbidity experienced with older age. The paper by L. Deckx et al. compares the chronic disease burden among cancer survivors aged 60 years and older with up to four controls matched for age, sex, and general practice, all drawn from a primary care database in the Netherlands. The results from this retrospective cohort study indicate similarly high levels of chronic disease among cancer patients prior to their diagnosis when compared with noncancer patients. The most common preexisting chronic diseases included diabetes, lipid disorders, ischaemic heart disease, and myocardial infarction, with only chronic obstructive pulmonary disease (COPD) significantly more prevalent among lung cancer patients. Among cancer survivors and noncancer patients, the incidence of chronic disease was again similar; venous thrombosis was more common in the two years after diagnosis in cancer survivors. Given their experience and expertise in managing multimorbidity, the authors emphasise the important role that general practitioners can have in supporting cancer survivors.

K. M. Bellizi et al. further examine the impact of age among cancer survivors in CA, USA, but extend the analysis to include the impact of race/ethnicity on health-related quality of life. The population-based questionnaire survey among adult survivors of breast, prostate, colorectal, ovarian, or endometrial cancer examined physical and mental function by age, ethnicity/race, and type of cancer, as well as potential interactions. The authors describe a double jeopardy in their study population, where a significant interaction effect between age and race/ethnicity impacting physical function is observed, persisting among older males with prostate cancer even after controlling for comorbidity. This is a salient reminder that not all older patients with cancer are alike in sociodemographic factors which may have had a profound effect on health status and on earlier stages of a patient's cancer journey are likely to continue to impact on health outcomes in the survivorship phase too.

Together, these papers highlight a number of important issues. Who are the elderly? There is no common definition across the papers with cutoffs of 60, 65, 70, 71 and, 75 years being used. These choices are largely pragmatic, reflecting the data sources available or the population in whom an intervention was being tested. However, it needs to be remembered that there are important differences within the "elderly." Not surprisingly, different responses to treatment are observed, increasing morbidity with age, and as noted above sociodemographic factors that shape the context of people's living experience remain important.

The importance of comorbidity and indeed multimorbidity comes through clearly with respect to treatment decisions and outcomes. Not all patients will benefit from treatment due to these other concomitant illnesses, or they may have less resilience to side effects, adversely impacting on quality of life. For patients who may already have a limited quality of life, the decision to undergo treatment is one that requires both clinical judgment and consideration of patient (and perhaps caregiver) preferences as well as contextual factors [8]. Good examples of such an approach exist, for example, [9]. Ideally, a multidisciplinary approach, including where appropriate the oncologist, general practitioner, geriatrician, cancer nurse specialist, and possibly the palliative care team, as well as the patient and family, will be adopted.

What should be the ongoing research agenda for this growing and challenging patient population? All aspects of the cancer control continuum (prevention, screening, detection and diagnosis, treatment, and survivorship) are relevant to older as well as younger patients, but the influence of age on many of these is still poorly understood.

Further work to identify which older patients might benefit from specific forms of cancer screening is needed [10], although the role of the general practitioner in this decision-making process is known to be important [11]. The influence of age and associated morbidities on the diagnostic accuracy of signs and symptoms or of diagnostic algorithms for specific cancer types and any subsequent differences in the diagnostic pathways in the elderly compared to those in younger cancer patients (including the impact, if any, of these differences) on the time of diagnosis and commencement of treatment requires further elucidation.

Further research is also needed on the role of patient preferences in determining treatment strategies following a diagnosis of cancer, optimal modes of information provision, and understanding determinants of patient suitability (physical and psychological) in the selection of appropriate therapy (whether chemotherapy, radiotherapy, surgery, and nonaggressive management). Better data on comparative outcomes of chemotherapy regimens, radiotherapy, and surgery between younger and older patients to guide both patients and providers is needed. Other areas meriting investigation include the effect of comorbidity on the response to treatment in elderly patients and the impact of a cancer diagnosis (and treatment) on psychological outcomes in elderly patients compared to younger patients.

The need for greater involvement of older people in cancer clinical trials has been recognised [12], but there is also a need for other research designs including qualitative ones where the voices of older people themselves—their attitudes towards health and treatment decisions—are heard.

Although not dealt with in this special issue, it is important too to remember the international context of the growing global burden of cancer among the elderly. More than half of new cancer diagnosis already occurs in less developed regions of the world; demographic changes including increasing life expectancy in many low- and middle-income countries will result in cancer (as well as other noncommunicable diseases)

giving rise to considerable health care challenges in the older population in this century. How cancer services are developed to address these is of growing concern [13, 14].

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Research Article

Undertreated Breast Cancer in the Elderly

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The effect of undertreatment with adjuvant hormonal therapy, chemotherapy, or radiation was studied in elderly women with breast cancer. A prospectively maintained database was used to identify women undergoing potentially curative surgery between 1978 and 2012. The presentation, pathologic findings, treatment, and outcomes of 382 women over 70 were compared to the findings in 2065 younger patients. Subsequently, conventionally treated and undertreated elderly patients were identified and their characteristics and outcomes were compared. Both young and old patients presented most frequently with mammographic findings, but older patients presented more frequently with mammographic masses while younger patients presented more frequently with mammographic calcifications. Cancers of older patients were significantly more favorable than cancers in younger patients: smaller, with more infiltrating lobular, fewer ductal carcinoma in situ, and more frequently estrogen receptor positive and fewer were poorly differentiated. Elderly patients had less axillary sampling, fewer mastectomies, less adjuvant radiation therapy, and more hormonal therapy. Fifty-one percent of the 382 elderly patients were undertreated by conventional criteria. Undertreated patients were more frequently in situ, better differentiated, smaller, and more often estrogen receptor positive. Forty-four percent of the undertreated patients died during followup without disease recurrence. Despite undertreatment, local and distant disease-free survival was comparable to patients who were not undertreated.

1. Introduction

The population of elderly individuals in the United States is increasing. Between 2000 and 2010 the population of women aged 65 and over increased by 11.3% with those 70 and over increasing by 6.4% [1]. According to the Surveillance Epidemiology and End Results (SEERs) database, from 2000 to 2009 the median age for breast cancer diagnoses in the USA was 61 years of age. Approximately 41% were diagnosed above the age of 65, of which 21% were above the age of 75 [2]. As the USA population of women over 65 increases, breast cancer in older individuals has and will continue to become more prevalent.

The management of breast cancer in the elderly has been a topic of debate. There is a lack of evidence on the optimal management of this group of patients secondary to low enrollment in randomized clinical trials [3, 4]. As a result, treatment decisions have been largely based on studies in younger patients which may not be applicable to elderly patients with breast cancer. Breast cancers in elderly women compared to younger women are histologically less aggressive and have a good response to hormonal therapy. This favorable biologic profile impacts the decision as to whether an elderly patient should be subjected to adjuvant therapy.

The consequences of these considerations are that elderly patients are often undertreated when compared to younger patients [5–7], but the question that needs to be answered is are there any clinical ramifications to the undertreatment of breast cancer in elderly women [6, 8, 9]? Diab and colleagues demonstrated that the impact of breast cancer on the expected survival of these elderly patients decreases with age [9] and the risk of dying from comorbid conditions often exceeds the risk of cancer recurrence and breast cancer mortality [10]. Although recommendations based on expert opinion are emerging, there is a paucity of level 1 evidence [11]. Determining the optimal treatment for an elderly patient depends largely on clinical judgement, weighing the patients' comorbid conditions with the biology of the tumor.

Table 1: Comparison of demographic variables in patients <71 years and ≥71 years.

Demographic variable	<71 y	≥71 y	*P* value
n	2065	382	
Age (y)	53	76	
Presentation	(*n* = 2065)	(*n* = 382)	
Palpable mass	766 (37%)	137 (36%)	<0.001
Mammographic calcium	471 (23%)	62 (16%)	
Mammographic mass	434 (21%)	138 (36%)	
Mammographic abnormality	27 (1%)	1 (0.26%)	
Other	367 (18%)	44 (12%)	
Mammography: positive/suspicious	1757/1869 (94%)	326/348 (94%)	0.813
Diagnostic method	(*n* = 1933)	(*n* = 363)	
Excisional biopsy	768 (40%)	157 (43%)	0.256
Fine-needle aspiration	445 (23%)	87 (24%)	
Core needle biopsy	720 (37%)	119 (33%)	

Data are presented as *n*, median, or *n* (%).

2. Methods

The senior author (P. I. Tartter) has created and maintained a breast cancer database with the followup of patients who have been cared for by him at Mount Sinai Hospital (1977–1999) or at St. Luke's-Roosevelt Hospital Center (1999–2012). Women 71 years of age and older at the time of diagnosis ($n = 382$) were identified and compared to women younger than 71 years of age at the time of diagnosis ($n = 2065$). We picked the age of 71 as a cutoff to facilitate comparison to other studies.

Data was collected on age, clinical presentation, mammographic findings, diagnostic method, histopathologic findings, tumor differentiation, tumor size, estrogen receptor status, axillary node status, resection margins, number of pathologically examined nodes, surgical treatment, re-excision, adjuvant hormone treatment, and chemotherapy and radiation therapy. Followup information was acquired from hospital and office records, patients, and their families. The last date of followup and the date of local or distant recurrence were recorded. The local and distant disease free survival rates were then calculated from the date of definitive surgery. For estimates of local and distant disease recurrence rates, patients in whom a recurrence did not develop were censored at the last followup or death, whichever occurred first.

Patients over 71 years of age who were undertreated by conventional criteria were compared to their appropriately treated counterparts. Our criteria for undertreatment included (1) omission of axillary sampling in patients with invasive tumors; (2) lack of postoperative radiation therapy in patients treated with breast conserving surgery; (3) lack of hormonal treatment in estrogen receptor positive patients with invasive cancers; (4) lack of chemotherapy in node-positive patients; (5) lack of chemotherapy in estrogen receptor negative patients with tumors larger than 2 cm.

The data was analyzed using SPSS software (SPSS Inc., Chicago, IL, USA) run on a Dell personal computer. The patients were divided into two groups by age (including the age of 71 and over or younger than age 71) and compared. The significance of differences in categorica variables was evaluated using chi-square test, and the significance of differences in continuous variables was evaluated using Student's *t*-test. Cumulative 5-year local and distant disease free survival rates were calculated using Kaplan-Meier method [12]. Cox's proportional hazards regression model was used to evaluate the relative prognostic significance of variables for both local and distant disease free survival [13].

3. Results

The 2,447 patients ranged in age from 22 to 96 years and 382 (16%) were of age 71 and above, considered elderly (Table 1). The 2,065 younger patients ranged in age from 22 to 70, with a median age of 53 and the patients over 70 years ranged in age from 71 to 96 years with a median age of 76. Most patients presented with a palpable mass (37%). Patients younger and older than 71 years were equally likely to have mammographic findings. Older patients presented more frequently with mammographic masses while younger patients presented more frequently with mammographic calcifications. Both the elderly and the younger patients were most commonly diagnosed by excisional biopsy followed by core needle biopsy and fine-needle aspiration.

Numerous significant differences were observed between the elderly and younger patients in terms of their pathology (Table 2). Older patients had significantly more infiltrating lobular cancers and fewer cases of ductal carcinoma in situ than younger patients and significantly fewer poorly differentiated cancers. The mean tumor size was significantly smaller in the elderly but the T stage distribution among the elderly and younger patients was comparable. Estrogen receptor positivity was more frequent among the elderly.

Axillary node sampling, sentinel node excision, or axillary dissection was more frequent in younger patients with removal of more lymph nodes with the proportionately more nodes involved with tumor. In addition to less aggressive treatment of the axilla, elderly patients also received less

Table 2: Pathologic findings in patients <71 years and ≥71 years.

Pathologic finding	<71 years	≥71 years	*P* value
Histopathology			
Infiltrating ductal	1408 (68%)	265 (69%)	0.028
Infiltrating lobular	164 (7.9%)	45 (12%)	
Ductal carcinoma in situ	424 (21%)	66 (17%)	
Unknown	69 (3.3%)	6 (1.6%)	
Tumor differentiation			
Well	319 (15%)	60 (17%)	0.000
Moderately	855 (41%)	207 (54%)	
Poorly	650 (31%)	84 (22%)	
Unknown	241 (12%)	31 (8.1%)	
Tumor size (cm)*			
Median	1.4	1.2	0.015
0–2	1428 (69%)	276 (72%)	0.250
2.1–5	398 (19%)	75 (20%)	
>5.1	117 (6%)	14 (3.7%)	
Unknown	122 (6%)	17 (4.5%)	
Node positive†	486/1524 (32%)	61/249 (25%)	0.027
Involved nodes†			
Mean	3.9	3.7	0.705
0	1137 (69%)	201 (76%)	0.066
1–3	320 (20%)	37 (14%)	
4+	180 (11%)	26 (10%)	
Estrogen receptor positive	1314/1702 (77%)	275/321 (86%)	<0.001
Initial resection margin: close/involved	751/1898 (40%)	225/353 (64%)	<0.001
Final Margin: close/involved	134/1863 (7.2%)	43/344 (13%)	0.002
Examined nodes (mean)	6.9	5.7	0.002
Axillary node sampling†	1524/1572 (97%)	249/310 (80%)	<0.001
Surgery			
Breast conservation	1529 (74%)	327 (86%)	<0.001
Mastectomy	519 (25%)	55 (14%)	
Unknown	17 (0.8%)	0 (0%)	
Neoadjuvant chemotherapy	280/1572 (18%)	20/310 (6.4%)	<0.001
Postoperative chemotherapy	517/1572 (33%)	23/310 (7.2)	<0.001
Tamoxifen/aromatase Inhibitor	1011/1809 (56%)	244/364 (67%)	<0.001
Tamoxifen among estrogen receptor positive patients	912/1217 (75%)	214/273 (78%)	0.231
Radiation therapy	1328/1442 (92%)	184/365 (50%)	<0.001
Radiation therapy in breast conservation	1232/1529 (81%)	173/327 (53%)	<0.001

Data are presented as *n* or *n* (%). (*Size of invasive component. †Invasive tumors).

aggressive surgical treatment of the breast: only 14% received mastectomies compared to 25% of younger patients.

Adjuvant therapy with both radiation and chemotherapy was significantly less frequent in the elderly while the use of Tamoxifen or an Aromatase inhibitor was more frequent. 81% of the 1,529 young patients treated with breast conservation received radiation therapy compared to 53% of the 327 elderly patients treated with breast conservation ($P < 0.001$). Among patients with invasive cancers, 18% of the young patients received neoadjuvant chemotherapy and 33% adjuvant chemotherapy compared to 6% and 7% of the comparable elderly patients ($P < 0.001$). The main form of systematic therapy for the elderly patients was hormonal: either Tamoxifen or Aromatase inhibitor. 67% of elderly patients were treated with hormonal therapy compared with 56% of younger patients ($P < 0.001$). Despite these differences, the elderly and younger patients had similar 5-year local and distant recurrence-free survival (Table 3).

Undertreated elderly patients were identified as described in Section 2. Undertreatment consisted of omission of radiation therapy in 154 of the 317 patients treated with breast conservation, omission of axillary node sampling in 61 of the 310 elderly patients with invasive cancers, omission of chemotherapy in 10 of 63 elderly patients with involved

Table 3: Local and distant disease-free survival.

Recurrence/age	n	Recurrence	Cumulative 5-year recurrence-free survival (%)	HR [95% CI]	P value*
Local recurrence					0.563
<71 year	2065	108	93	1 [reference]	
≥71 year	382	23	92	0.95 [0.63–1.45]	
Distant recurrence					0.464
<71 year	2065	168	89	1 [reference]	
≥71 year	382	24	91	1.05 [0.75–1.48]	

*P value is from log-rank test comparing Kaplan-Meier survival curves.

nodes, and omission of hormonal therapy in 59 of 321 elderly patients with estrogen receptor positive cancers. By these criteria many patients were undertreated with more than one modality. As a consequence, 190 (51%) of the elderly patients were undertreated with at least one modality. Undertreated elderly patients were significantly older than their appropriately treated counterparts (77 versus 75, $P < 0.001$). The cancers of the undertreated elderly were more frequently in situ, better differentiated, smaller, and more often estrogen receptor positive (Table 4). Reflecting the criteria used to identify undertreated patients, one-third did not receive axillary sampling for invasive cancers, two-thirds did not receive radiation, almost half did not receive hormonal therapy, and a few received chemotherapy. Despite these differences in treatment, elderly undertreated patients generally fared as well as the appropriately treated elderly (Table 5). Equal numbers of patients in both groups developed local recurrences resulting in five-year cumulative local disease-free rates of 93% for the appropriately treated and 91% for the undertreated. 9% of the 167 appropriately treated elderly patients with invasive cancers developed distant disease compared to 4% of undertreated patients causing the cumulative five-year distant disease free rate to be 89% in appropriately treated patients compared to 93% in the undertreated one. It is important to note that 44% of the 190 undertreated elderly died without disease recurrence compared to 29% of the appropriately treated patients ($P < 0.001$).

A Cox regression model was used to evaluate potential prognostic factors such as tumor pathology, differentiation, size, number of involved nodes, estrogen receptor status, and treatment with chemotherapy, hormonal therapy, and radiation, among the elderly patients (Table 6). Local disease-free survival was significantly related to estrogen receptor status ($P < 0.001$) and pathology ($P = 0.043$). Twenty-four percent of the 46 patients with estrogen receptor negative cancers developed local recurrence within five years compared to 3% of the 275 patients with estrogen receptor positive tumors. The cumulative five-year risk of local recurrence in patients with ductal carcinoma in situ was 4% (2/66) compared to 10% (3/45) in patients with invasive lobular cancers and 9% (18/266) in patients with invasive ductal cancers. Among patients with invasive cancers, tumor size ($P = 0.006$), number of involved nodes ($P < 0.001$), and estrogen receptor status ($P = 0.008$) were significantly related to distant recurrence. Undertreatment was not significantly related to local or distant recurrence in univariate or multivariate analysis.

Undertreatment with radiation in elderly patients that underwent breast conservation was associated with increased risk of local recurrence. Five-year local disease-free survival of the unirradiated patients was 90% compared to 96% for the irradiated patients ($P = 0.450$). The cumulative five-year distant disease free survival of patients receiving chemotherapy was 73% compared to 93% for patients not receiving chemotherapy ($P = 0.004$). This difference is attributable to the larger, more poorly differentiated cancers with more positive nodes among patients receiving chemotherapy. Omission of hormonal therapy in estrogen receptor positive patients resulted in a lower distant disease free survival: 91% of estrogen receptor patients treated without hormonal therapy were without distant metastases at five years compared to 94% of patient using hormonal therapy.

4. Discussion

This study found that elderly patients with breast cancer present with palpable masses and mammographic findings similar to younger patients, although mammographic masses were more frequent in the elderly and mammographic calcifications were more frequent among the young patients. Cancers of the elderly tended to be less often in situ than in younger patients but invasive cancers were generally smaller, better differentiated, more frequently estrogen receptor positive, and with less nodal involvement. Older patients were treated less aggressively than younger patients. They received fewer mastectomies, less radiation after breast conservation, and very seldom did they receive chemotherapy even for node-positive cases. Elderly patients received hormonal therapy as frequently as younger patients. Despite often being undertreated, elderly patients experienced outcomes comparable to younger patients presumably because their cancers were smaller, better differentiated, and with fewer involved nodes.

More than one-half of our elderly patients were also undertreated according to current breast cancer treatment guidelines: omission of axillary sampling in patients with

Table 4: pathologic findings in undertreated and properly treated aged ≥71 years.

Pathologic finding	Full treatment	Undertreated	*P* value
Histopathology			
Infiltrating ductal	149 (80%)	114 (60%)	<0.001
Infiltrating lobular	18 (10%)	25 (13%)	
Ductal carcinoma in situ	15 (8%)	51 (27%)	
Unknown	4 (2.2%)	0 (0%)	
Tumor differentiation			
Well	26 (14%)	35 (18%)	<0.001
Moderately	91 (49%)	113 (59%)	
Poorly	57 (31%)	24 (13%)	
Unknown	12 (6.5%)	18 (9.5%)	
Tumor size (cm)*			
Median	1.4	1.0	0.003
0–2	128 (69%)	146 (77%)	0.169
2.1–5	41 (22%)	32 (17%)	
>5.1	8 (4.3%)	4 (2.1%)	
Unknown	9 (4.8%)	8 (4.2%)	
Involved nodes†			
Mean	1.1	0.5	0.021
0	119 (75%)	80 (81%)	0.103
1–3	19 (12%)	14 (14%)	
4+	21 (13%)	5 (5%)	
Estrogen receptor positive	133/162 (82%)	140/155 (90%)	0.034
Final margin: close/involved	19/166 (11%)	23/175 (13%)	
Examined nodes (mean)	8	3	<0.001
Axillary node dissections†	153/167 (92%)	90/139 (65%)	<0.001
Surgery			
Breast conservation	151 (81%)	167 (88%)	0.091
Mastectomy	34 (18%)	23 (12%)	
Unknown	1 (0.5%)	0 (0%)	
Postoperative chemotherapy	43/184 (23%)	5/190 (3%)	<0.001
Tamoxifen	142/181 (78%)	98/183 (54%)	<0.001
Radiation therapy	155/184 (84%)	29/89 (33%)	<0.001

Data are presented as *n* or *n* (%).
*Size of invasive component.
†Invasive tumors.

Table 5: Local and distant disease-free survival in undertreated and properly treated patients aged ≥71 years.

Recurrence/treatment	*n*	Recurrence	Cumulative 5-y recurrence-free survival (%)	HR [95% CI]	*P* value*
Local recurrence					0.847
Undertreated	190	11	91	1 [reference]	
Properly treated	185	11	93	0.79 [0.33–1.92]	
Distant recurrence (invasive cancer)					0.155
Undertreated	139	6	93	1 [reference]	
Properly treated	167	15	89	2.03 [0.86–4.80]	

*P value is from log-rank test comparing Kaplan-Meier survival curves.

Table 6: Cox regression of potential prognostic factors in patients over 70 (P values).

Variable	Local recurrence	Distant recurrence
Histopathology	0.043	0.702
Tumor differentiation	0.855	0.571
Tumor size (cm)	0.520	0.006
Involved nodes[†]	0.306	<0.001
Estrogen receptor positive	<0.001	0.008
Postoperative chemotherapy	0.517	0.198
Tamoxifen	0.091	0.375
Radiation therapy	0.620	0.375
Undertreatment	0.150	0.818

[†] Invasive tumors.

invasive cancers, omission of radiation in patients treated with breast conservation, omission of chemotherapy in patients with involved nodes, or omission of hormonal therapy in patients with estrogen receptor positive cancers. Despite the large number of undertreated patients, there were no significant differences in local or distant disease free survival among undertreated and appropriately treated patients.

Previous studies of elderly patients with breast cancer have not universally observed that cancers in the elderly are biologically more favorable and less advanced than those seen in younger patients. This is in part due to differences in the populations studied. Generally when one compares the cancers of patients over 70 to patients between 50 and 70, differences are not striking [14, 15]. However, if one includes all patients younger than 70, the more favorable biology becomes more apparent [16]. In addition, many studies included elderly patients who were not treated with surgery for a variety of reasons including comorbidity, advanced disease, and patient refusal [17–20]. All of the patients in the current study were potentially curable at presentation; all had surgery, and no stage IV patients are included. A universal finding in all the studies is the increasing frequency of estrogen receptor positivity with increasing age. This usually results in the increased use of hormonal therapies in the elderly.

Undertreatment of the elderly is also a universal finding. In fact several authors have found that undertreatment, that is, lack of adherence to guidelines, is frequent at all ages [14]. The controversy that exists is whether undertreatment of patients, particularly the elderly, results in adverse outcomes. There is no question that radiation therapy reduces local recurrence rates after breast conservation for invasive and in situ disease regardless of the patient's age. However, a reduction of 3% in local recurrence does not significantly benefit an 80-year-old woman with a life expectancy of ten years who has only a 50% chance of experiencing the benefit of radiation therapy [21]. Another consideration is that patients who are not irradiated and develop local recurrences may be candidates for relumpectomy with or without radiation therapy, whereas patients who develop local recurrences after treatment with radiation should undergo mastectomy.

Previous studies noted that elderly patients with invasive cancers experience higher mortality when axillary dissection is omitted [22]. Among these studies, a few measured breast cancer specific survival. It is likely that patients not undergoing axillary dissection have higher comorbidities causing the higher mortality, not that the omission of axillary surgery caused the higher mortality. The recently completed trial randomizing patients with involved sentinel nodes to completion axillary dissection versus no additional surgery showed no benefit for completion axillary dissection [23].

Finally, with respect to chemotherapy, a few elderly patients are willing to participate in randomized trials with chemotherapy arms and a few are willing to accept chemotherapy even with relatively advanced disease [3, 4, 24, 25]. Only 36 of our elderly patients were estrogen receptor negative and 13 of these had nodal involvement. All received chemotherapy and an additional 11 patients with node negative estrogen receptor negative larger cancers received chemotherapy. Because of the small numbers of patients and the association of chemotherapy with advanced estrogen receptor negative disease, patients receiving chemotherapy fared worse than patients not receiving chemotherapy.

This study has several limitations. It is a retrospective single surgeon database review and thus carries the inherent limitations of an observational study. This includes a potential physician bias and bias as a result of confounding by indication. It must be mentioned, however, that in today's world of cancer treatment, care is individualized and the patient ultimately determines what treatment she is to receive. A larger multicenter, prospective randomized trial of adherence to guidelines for the treatment of breast cancer in elderly patients would be needed to overcome these biases. This trial, however, is unlikely to occur and probably does not need to. Breast cancer in elderly patients has a favorable biological profile and therefore treatment does not need to fall under the confines of traditional guidelines. Moreover, coupled with comorbid conditions that are frequently encountered as people age, optimal treatment should be determined largely by clinical judgement on a case by case basis. It is known that elderly patients are undertreated but this study did not find that the omission of conventional surgery or adjuvant therapies adversely affected outcome among patients over 71 years of age.

Conflict of Interests

The authors do not have any conflict of interests to disclose.

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Research Article

Uptake and Tolerance of Chemotherapy in Elderly Patients with Small Cell Lung Cancer and Impact on Survival

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The treatment of elderly cancer patients is complicated by many factors. We sought to assess the uptake and tolerance of chemotherapy among patients 75 years and older diagnosed with small cell lung cancer (SCLC) in years 2004–2008 in Alberta, Canada, and assess their survival. All patients who met the above criteria and had an oncologist-consult were included. Data were obtained from the Alberta Cancer Registry and chart review. A total of 171 patients were included in the study, 117 (68%) of whom began chemotherapy. Of those, 52% completed all cycles, 66% did not have any dose reductions, and 31% completed all cycles at the recommended dose. The risk of death for patients who did not complete all cycles of chemotherapy was 2.72 (95% CI: 1.52–4.87) and for those who completed all cycles but with a reduced dose was 1.02 (95% CI: 0.57–1.82) relative to those who completed chemotherapy at full dose after adjusting for several demographic/clinical factors. Our results suggest that a significant proportion of elderly patients are able to tolerate chemotherapy and receive a survival benefit from it while those who experience toxicity may receive a survival benefit from a reduction in chemotherapy dose as opposed to stopping treatment.

1. Introduction

Lung cancer is the leading cause of cancer-related death in developed nations [1]. Small cell lung cancer (SCLC) accounts for 13–20% of all lung cancer diagnoses and is commonly classified into two stages, limited and extensive, according to the Veteran's Administration Lung Cancer Study Group (VALG) classification system [2]. This system is used because most SCLC patients present at a stage for which surgery is not appropriate, and thus are usually unable to be classified by the more commonly used cancer staging classification system, tumor-node-metastasis (TNM), which requires surgical confirmation to achieve an accurate classification [3].

SCLC is characterized generally by a rapid growth rate, initial sensitivity to chemotherapy and radiation, and early metastasis to regional lymph nodes and/or distant sites [3]. Limited SCLC is generally described as disease limited to one hemithorax, while extensive SCLC is described as disease present in both hemithoraxes and/or metastasized to more distant areas of the body. Those with limited stage SCLC have a better prognosis than those with extensive stage disease. The median survival for limited SCLC patients is 23 months, while those with extensive SCLC have a median survival of 8–12 months, if treatment is administered [4]. Over 50% of lung cancer patients in Canada are diagnosed at 70 years of age or older while over 20% are diagnosed at age 80 years or older [5].

The standard of care for patients with SCLC combined concurrent chemoradiotherapy for those with limited disease and chemotherapy alone for those with extensive disease [6]. The preferred chemotherapy regimen is etoposide plus cisplatin; however, etoposide plus carboplatin is an acceptable alternative for patients who are unable to tolerate cisplatin. Many elderly SCLC patients are not selected to receive chemotherapy, however, for fear of toxicity due to

their age and the presence of comorbidities [7, 8]. It is also recommended that patients who have achieved remission or stable disease after the completion of primary treatment receive prophylactic cranial radiation (PCI) to reduce the risk of brain metastases [6]. Additionally, if a patient is not a good candidate for or refuses chemotherapy, they may receive radiation to symptomatic sites.

Evidence-based care for the elderly lung cancer population is lacking due to the underrepresentation of this population in clinical trials [9]. Cancer trials tend to consider 70 years of age as the reference point for being "elderly;" however, there is not a specific minimum age that clearly defines the term [10]. The tendency to exclude elderly patients from cancer treatment clinical trials on the basis of chronological age is largely because older patients are more likely to have serious comorbid conditions and have reduced organ function which can lead to higher drug-related toxicities [11–14]. Many elderly people, however, do not have any measurable loss of functional capacity and are free from significant medical problems [15]. In Canada, it has been estimated that 45% of those 75–84 years of age and 22% of those 85 years of age and older are in "overall good health" [16]. In addition, studies have shown that age alone is not significantly associated with adverse prognosis [7, 17]. This suggests that elderly patients should not be excluded from therapeutic opportunities solely on the basis of age [18, 19].

The care of elderly patients is, however, often complicated by comorbidities, frailty, and decreased organ function. The purpose of this study was to describe the receipt of chemotherapy provided to elderly patients with SCLC in Alberta, Canada, and assess their chemotherapy tolerance and survival. We also sought to identify the reasons for not recommending chemotherapy and for dose reductions and assess the relationship of patient age in these decisions. In the absence of clear evidence from clinical trials, the analysis of the elderly SCLC population through retrospective population-based studies such as this one helps assess and quantify the value of treating elderly cancer patients with chemotherapy.

2. Methods

A retrospective, population-based study was conducted on all residents of Alberta, Canada, diagnosed with SCLC at the age of 75 years or older in years 2004–2008 who had an oncologist-consult. Selection of 75 years was chosen because the median patient age for SCLC in Alberta is about 70 years, and we wanted to focus on the "significant minority" of elderly patients. Furthermore, on basis of our clinical experience, we felt that patients who are 75 years and older are the ones for whom ideal treatment is the least clear; we, therefore, selected 75 years as the age cut-off. The province of Alberta consists of an area of 660,000 km^2 and has a population of 3.7 million. Approximately 80% resides in urban areas [20].

The healthcare system in Alberta is funded and administered publically, as it is throughout all of Canada; standard cancer care such as consultations with specialists and chemotherapy is free to residents. Cancer care is organized and coordinated provincially. Consultations with oncologists, nonsurgical cancer treatment, and other services are provided at cancer care facilities. Prior to receiving chemotherapy, a patient must be referred to one of six cancer facilities in the province to have a consultation with an oncologist with whom treatment options are discussed. Two of these cancer facilities are located in the major cities of Edmonton and Calgary; the remaining four are located in smaller cities. Chemotherapy can be provided through any one of the 17 provincial cancer care facilities.

The Alberta Cancer Registry was used to identify patients 75 years of age or older diagnosed with SCLC (International Classification of Diseases for Oncology (ICD-O-3) [21] topography codes C34.0–C34.9 and morphology codes 8040–8045) in years 2004–2008. Patients were excluded if they were not residents of Alberta, were diagnosed with combined small cell and nonsmall cell lung cancers, or had another cancer diagnosis for which they were receiving treatment. Gender, date of birth, and date of death were also obtained from this source. The Alberta Cancer Registry has been repeatedly recognized by the North American Association of Central Cancer Registries (NAACCR) for its high level of completeness and for the timeliness of its data reporting [22].

A chart review was conducted on all potentially eligible patients identified from the cancer registry to identify those who had an oncologist-consult and to obtain details of the chemotherapy received. All patients who had an oncologist-consult were included in the study. The following data were extracted from patient charts: cancer stage; presence and type of comorbidities; Eastern Cooperative Oncology Group (ECOG) performance status; whether or not chemotherapy was recommended by the oncologist; reasons for not recommending chemotherapy; whether chemotherapy was administered or patient refused reasons patient refused chemotherapy; chemotherapy start date; treatment regimen received; whether the patient received all chemotherapy cycles; number of cycles received if less than the complete amount; reasons for incomplete chemotherapy cycles; whether dose reduction occurred; reasons for dose reduction and changes to the initially recommended chemotherapy regimen. A complete course of chemotherapy was defined as receiving any of the regimens once every three weeks for 4 cycles. Dose reduction was defined as any reduction in the dose of chemotherapy administered to the patient, compared to the recommended dose; dose reduction that occurred at any time during chemotherapy treatment, including the first cycle, was included. Information about other treatments received, such as radiation or second-course treatment, were not collected; however, it is likely that most, if not all, patients with limited stage disease who received chemotherapy also received radiation. Patients with extensive stage disease, however, would only have received radiation to relieve symptoms; such treatment is palliative and would not impact survival.

This study was reviewed and approved by the Alberta Cancer Research Ethics Committee.

2.1. Data Analysis. Descriptive statistics were calculated to describe the utilization and tolerance of chemotherapy in the SCLC patients who had an oncologist-consult. Exploratory data analyses were performed to determine cut-off values for continuous variables and to assess the relationships of these variables with commencing chemotherapy, dose reductions, and not completing all chemotherapy cycles. Chi-square test or Fisher's exact test (if the expected value of a cell was less than 5) were performed to assess the statistical significance of these associations.

Kaplan-Meier (K-M) curves were generated to compare patient survival by age (<80 versus ≥80) and treatment completeness status. In order to ensure chemotherapy, completeness status was known at the beginning of the time period; the start time (T0) was defined as 12 weeks after the oncologist-consult; all patients were followed to the earlier of their death date or December 31, 2010. The log-rank test and the Wilcoxon test were used to determine statistical differences between the curves. The statistical software R was used to generate the K-M graphs.

Cox proportional hazard models were used to estimate the effect of treatment status on patient survival, adjusting for ECOG score, disease stage, age at diagnosis, number of comorbidities, and chemotherapy regimen used. As in the K-M graphs, the start time (T0) was defined as 12 weeks after the oncologist-consult date in order to categorize patients properly for chemotherapy completion and dose reduction statuses. The Wald Chi-square test was used to calculate P values for the hazard ratio estimates. All P values are based on two-sided tests. SAS software (version 9.2; SAS Institute, Cary, NC, USA) was used to perform all analyses.

3. Results

There were 238 patients aged 75 years or older diagnosed with SCLC in Alberta, Canada, in years 2004 to 2008. Of these, 11 were excluded for the following reasons: 2 were not residents of Alberta; 7 had a diagnosis of combined non-small cell and small cell lung cancer; and 2 had another cancer diagnosis for which they were receiving treatment. Of the remaining 227 potentially eligible patients, 171 (75%) had an oncologist-consult to discuss treatment options and were included in this study. There were 56 patients (25% of those potentially eligible for this study) who did not have an oncologist-consult. Relative to the patients who had an oncologist-consult, those who did not tend to be older (46% were older than 80 years compared to 35%). Additionally, almost half of them (46%) died within two weeks of their diagnosis.

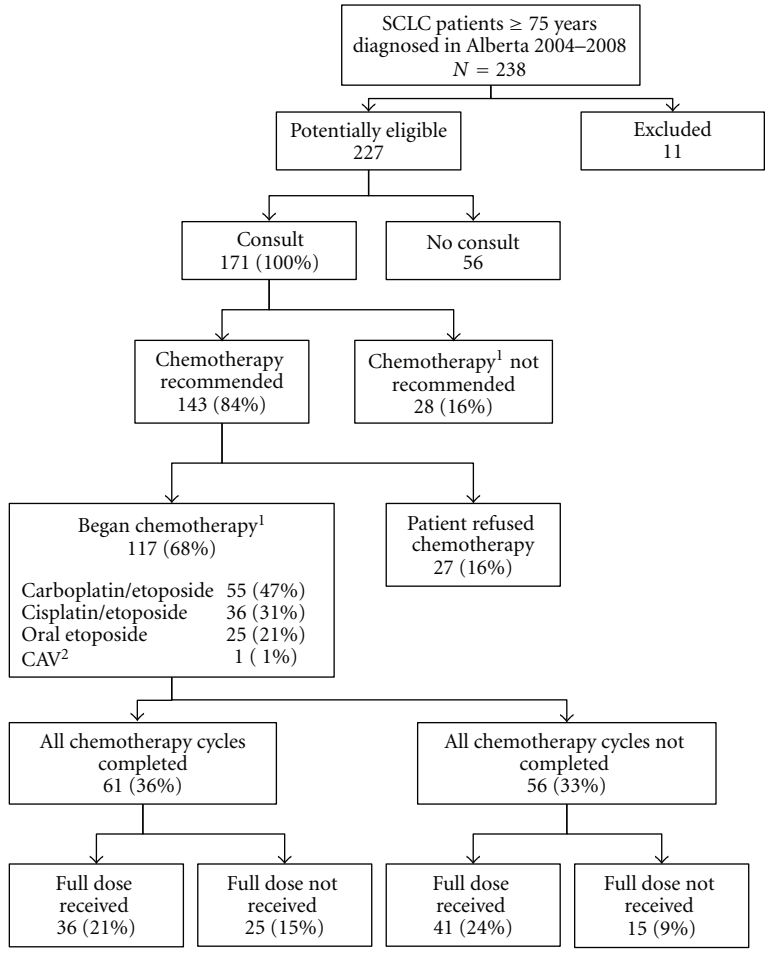
Figure 1 shows a flow chart of the proportion of patients for whom chemotherapy was recommended, began chemotherapy, refused it, received regimen, completed chemotherapy, and who received versus who did not receive chemotherapy cycles at the full dose. Of the patients who had an oncologist-consult, 84% were recommended chemotherapy and 68% began chemotherapy (including one patient who commenced chemotherapy despite the fact it is not recommended). The chemotherapy regimens received were cisplatin/etoposide, carboplatin/etoposide, cyclophosphamide/adriamycin/vincristine (CAV), and oral etoposide. The regimens most frequently used were combinations carboplatin/etoposide (47%) and cisplatin/etoposide (31%). Of those who began chemotherapy, 52% completed all cycles, 66% did not have any dose reductions, and 31% completed all cycles at the recommended dose. Of those who completed all cycles of chemotherapy, 34% had limited stage disease.

The relationship between the demographic and clinical characteristics of the patients included in the study and age is shown in Table 1. Just over half of the patients in both age groups were male, and 77% had extensive disease. A higher percentage of patients 80 years and older had an ECOG score of 3 or 4 compared to those 75–79 years, 47% versus 39%, respectively, $P = 0.18$. Patients 80 years and older were more likely to have two or more comorbidities than those aged 75–79, 62% versus 48%, respectively.

Table 2 displays the demographic and clinical characteristics of the patients included in the study and the relationship between those characteristics and beginning chemotherapy, having a dose reduction, and incomplete chemotherapy cycles. Of the patients included in the study, 57% were male, 35% were 80 years or older, 77% had extensive disease, 42% had an ECOG score of 3 or 4, and 24% had 3 or more comorbidities. A higher percentage of patients aged 75–79 received chemotherapy than those 80 years or older, 74% versus 58%, respectively, $P = 0.15$. Of those who received chemotherapy, a higher percentage of patients 80 years or older had dose reductions than those 75–79 years, 46% versus 29%, respectively, $P = 0.09$. Just over half of patients in both age groups, however, received all cycles of chemotherapy. Patients with limited disease were more likely to receive chemotherapy than those with extensive disease (87% versus 63%, $P = 0.02$); of those who received chemotherapy, 52% (43 patients) with extensive disease did not complete all chemotherapy cycles compared to 36% (12 patients) with limited stage disease, $P = 0.13$. Similarly, patients with a poor performance status (ECOG 3 or 4) were less likely than those with a good performance status to complete all cycles of chemotherapy, 65% versus 37%, $P = 0.007$.

Of those who had an oncologist-consult, 28 patients (16%) were not recommended chemotherapy, and 27 patients (19%) for whom chemotherapy was recommended refused it. Oncologists' reasons for not recommending chemotherapy and patients' reasons for refusing it are listed in Table 3. The most common reason oncologists indicated for not recommending chemotherapy was patient performance status (22 of 28 patients). The second most common reason was the presence of comorbidities (16 of 28 patients). Most patients who refused chemotherapy did so due to concerns about toxicity (20 of 27 patients).

Of those who began chemotherapy, 33% had a dose reduction, and 48% did not complete all treatment cycles. The most common reason for dose reduction was hematological toxicity (30 of 40 patients), while 10 of 40 patients had a dose reduction due to frailty and performance status (Table 4). Similarly, receipt of an incomplete number of chemotherapy cycles was largely attributable to



(1) One patient commenced chemotherapy for whom it was not recommended
(2) CAV = cyclophosphamide, adriamycin, vincristine

Figure 1: Flow chart of the number of patients included in the study, had a consult, were recommended chemotherapy, received it, and completed it.

hematological toxicity (32 of 56 patients), concerns regarding frailty and performance status (25 of 56 patients), and non-hematological toxicity (19 of 56 patients).

Table 5 outlines the drug regimens received and the number of cycles completed by treatment status. Patients who received the carboplatin/etoposide regimen were twice as likely to have dose reductions as those who received oral etoposide, 44% versus 20%, respectively, $P = 0.13$. Conversely, those who received the oral etoposide regimen were more likely to receive an incomplete number of chemotherapy cycles than those who received the combined etoposide/platin-based regimens, 64% versus 43%, respectively, $P = 0.05$. Of those who began chemotherapy, 61 patients (52%) completed all cycles; 25 (41%) of those who completed all cycles had a dose reduction. A large proportion (26%) of people who began chemotherapy only completed one cycle even though 20% of these people received it at a reduced dose.

All but four patients died by the end of the follow-up period, December 31, 2010. Lung cancer was the recorded cause of death for all patients with the exception of 14; 13 patients died of a noncancer related cause, and one patient died of prostate cancer. Figure 2 displays K-M survival curves by chemotherapy cycle completion status (complete versus incomplete/did not receive) and age group (75–79 versus 80 or older). Those who completed chemotherapy had a better survival rate than those who did not ($P < 0.0001$). The median survival for those who did not complete chemotherapy was 3 months and 23 days, compared to 7 months and 13 days for those who completed all cycles. The survival rate of those who completed chemotherapy did not differ by age group ($P = 0.21$).

Table 6 presents the results from the adjusted survival analysis, generated from the Cox proportional hazards model. Treatment status was the factor most strongly associated with survival. The risk of death for patients who did not complete all cycles of chemotherapy was 2.72 (95% confidence interval: 1.52 to 4.87) relative to those who completed chemotherapy at full dose after adjusting for other variables ($P = 0.0007$). The risk of death for patients who

Table 1: Association of demographic/clinical characteristics and age of patients diagnosed with SCLC who had an oncologist-consult.

		Age at diagnosis 75–79 years *N* (%)	Age at diagnosis 80 years and older *N* (%)
Total		111	60
Sex	$P = 0.53$		
Male		61 (55)	36 (60)
Female		50 (45)	24 (40)
Stage	$P = 1.00$		
Extensive		85 (77)	46 (77)
Limited		25 (23)	13 (22)
Unknown		1 (1)	1 (2)
ECOG	$P = 0.18$		
0, 1, and 2		51 (46)	19 (32)
3 and 4		43 (39)	28 (47)
Missing		17 (15)	13 (22)
Number of co-morbidities	$P = 0.12$		
0		13 (12)	3 (5)
1		44 (40)	20 (33)
2		26 (23)	24 (40)
≥3		28 (25)	13 (22)

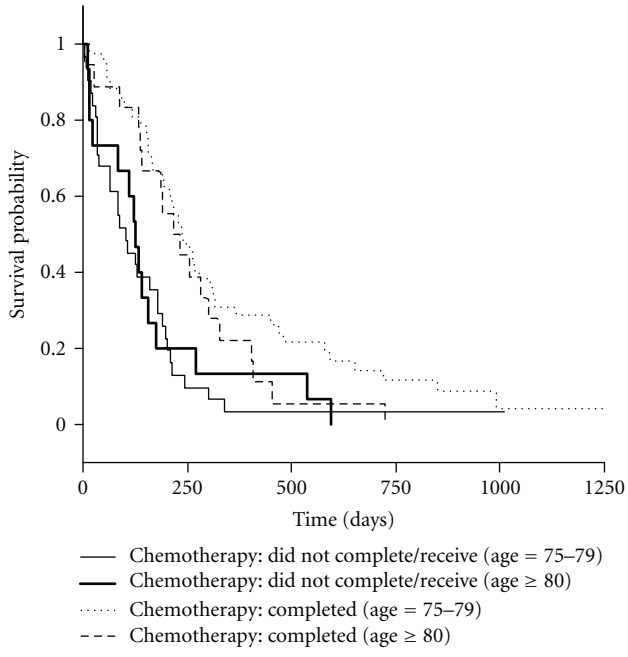


Figure 2: Kaplan-Meier survival curves of all SCLC patients who had an oncologist-consult by chemotherapy completion status, where T0 is 12 weeks after consult.

completed treatment at a reduced dose did not differ from those who completed chemotherapy at the full dose (HR = 1.02, 95% confidence interval: 0.57 to 1.82, $P = 0.94$). Due to the overlapping confidence intervals between the "Completed/reduced dose" group and the "Not completed" group, the model was rerun using the "Completed/reduced dose" group as the reference. In this analysis, the risk of death for patients who did not complete chemotherapy was 2.67 (95% confidence interval: 1.45 to 4.91, $P = 0.0016$) similar to the results shown in Table 6 using the "Completed/full dose" group as the reference.

4. Discussion

The purpose of this study was to describe the uptake and tolerance of chemotherapy among elderly patients with SCLC and assess their survival. Thirty-five percent of our study population was aged 80 years and older. These elderly patients, compared to those 75–79 years of age, received less chemotherapy and were more likely to receive a dose reduction, but were equally likely to complete all chemotherapy cycles. Notably, the adjusted hazard ratio of death did not differ between the two age groups. Overall, 52% of patients who began chemotherapy completed all cycles, and 41% had reduced chemotherapy doses. These results are confirmation that a significant proportion of elderly patients are able to tolerate chemotherapy and receive a survival benefit from it even in the presence of dose reductions.

Our results also suggest that elderly patients who have their chemotherapy dose reduced but complete all chemotherapy cycles have a similar survival (HR 1.02, CI 0.57–1.82) to those who complete all chemotherapy cycles at the full dose, after adjusting for ECOG score, disease stage, age, co-morbidity count, and drug regimen. Several phase II clinical trials have tested the efficacy of lower dose combinations of concurrent carboplatin and etoposide regimens in elderly SCLC patients [23–26]. Despite some differences

Table 2: Association of demographic/clinical characteristics and receipt/tolerance of chemotherapy of patients diagnosed with SCLC aging 75 years and older who had an oncologist-consult.

	Consult with an oncologist	Began chemotherapy	Dose reduction	Incomplete chemotherapy cycles
	N (%)[1]	*N* (%)[2]	*N* (%)[3]	*N* (%)[3]
Total	171 (100)	117 (68)	40 (34)	56 (48)
Sex		$P = 0.53$	$P = 0.34$	$P = 0.20$
Male	97 (57)	66 (68)	25 (38)	35 (53)
Female	74 (43)	51 (69)	15 (29)	21 (41)
Age at diagnosis		$P = 0.15$	$P = 0.09$	$P = 0.76$
75–79	111 (65)	82 (74)	24 (29)	40 (49)
≥80	60 (35)	35 (58)	16 (46)	16 (46)
Year of diagnosis		$P = 0.19$	$P = 0.90$	$P = 0.08$
2004	32 (19)	17 (53)	6 (35)	3 (18)
2005	35 (20)	28 (80)	8 (29)	17 (61)
2006	36 (21)	24 (67)	9 (38)	13 (54)
2007	36 (21)	23 (64)	7 (30)	11 (48)
2008	32 (19)	25 (78)	10 (40)	12 (48)
Stage		$P = 0.02$	$P = 0.78$	$P = 0.13$
Extensive	131 (77)	83 (63)	28 (33)	43 (52)
Limited	38 (22)	33 (87)	12 (36)	12 (36)
Unknown	2 (1)	1 (50)	0 (0)	1 (100)
ECOG		$P = 0.23$	$P = 0.18$	$P = 0.007$[4]
0, 1 and 2	70 (40)	59 (84)	24 (41)	22 (37)
3 and 4	71 (42)	40 (56)	11 (28)	26 (65)
Missing	30 (18)	18 (60)	5 (28)	8 (44)
Number of co-morbidities		$P = 0.84$[4]	$P = 0.51$[4]	$P = 0.89$[4]
0	16 (9)	13 (81)	5 (38)	7 (54)
1	64 (38)	41 (64)	16 (39)	18 (44)
2	50 (29)	30 (60)	8 (27)	16 (53)
≥3	41 (24)	33 (80)	11 (33)	15 (45)

[1]Column percentage.
[2]Row percentage: denominator is the number who had a consult in corresponding row.
[3]Row percentage: denominator is the number who began chemotherapy in corresponding row.
[4]*P* values based on Cochran-Armitage test for trend.

Table 3: Oncologists' reasons for not recommending chemotherapy and patients' reasons for refusing chemotherapy.

	Reasons for not recommending chemotherapy[1]	Reasons for patients' refusal of chemotherapy[1]
	N (%)[2]	*N* (%)[2]
Total	28 (100)	27 (100)
Performance status	22 (79)	3 (11)
Co-morbidities	16 (57)	4 (15)
Toxicity	0 (—)	20 (74)
Lack of social network or support	1 (4)	2 (7)
Wound healing problems	1 (4)	0 (—)
Age	0 (—)	2 (7)
Transportation issues	0 (—)	1 (4)
Other reasons	0 (—)	4 (15)
Unclear	4 (14)	4 (15)

[1]The oncologist or patient could have multiple reasons; therefore, the sum of each reason exceeds the total number in each column.
[2]Column percentage.

Table 4: Reasons for dose reduction and not completing chemotherapy.

	Reasons for dose reduction[1]	Reasons for incomplete chemotherapy cycles[1]
	N (%)[2]	*N* (%)[2]
Total	40 (100)	56 (100)
Hematological toxicity	30 (75)	32 (56)
Nonhematological toxicity	3 (8)	19 (34)
Frailty/performance status	10 (25)	25 (44)
Other medical reason	5 (13)	13 (25)
Patients' decision	0 (—)	2 (4)
Unclear	6 (15)	8 (14)

[1]Multiple reasons are possible; therefore, the sum of the reasons exceeds the total in each column.
[2]Column percentage.

Table 5: Drug regimen received and number of cycles completed by treatment status.

	Began chemotherapy *N* (%)[1]	Dose reduction *N* (%)[2]	Incomplete chemotherapy cycles *N* (%)[2]
Total	117 (100)	40 (34)	56 (48)
Drug regimen		$P = 0.13$[3]	$P = 0.05$[3]
Carboplatin/etoposide	55 (47)	24 (44)	27 (49)
Cisplatin/etoposide	36 (31)	11 (31)	12 (33)
oposide	25 (21)	5 (20)	16 (64)
CAV	1 (1)	0 (0)	1 (100)
Numbers of cycles completed			
1	30 (26)	6 (20)	
2	12 (10)	4 (33)	
3	14 (12)	5 (36)	
4+[4]	61 (52)	25 (41)	

[1]Column percentage.
[2]Row percentage: denominator is the number who began chemotherapy in corresponding row.
[3]*P* values based on Fisher's exact test.
[4]Defined as completed chemotherapy cycles.

in treatment schedule and dosing, three of these studies reported similar survival results as the usual treatment regimen, with a median survival of 41–46 weeks. One of these studies reported lower median survival, however, with a median survival of 37 weeks [26]. Further investigation is, therefore, warranted to better assess the relationship between chemotherapy dose reduction and survival of elderly SCLC patients.

A larger study similar to ours which included a population-based group of elderly SCLC patients was conducted in The Netherlands [27]. The most common reasons for not receiving chemotherapy were a combination of age, co-morbidity, poor performance status, and refusal by the patient or family, which are similar reasons as those identified in our study. They found that 53% of SCLC patients received chemotherapy, which is also similar to the 52% of potentially eligible patients from our study that received chemotherapy. As well, a similar percentage of patients had a dose reduction (30% versus 34%) and were unable to complete all chemotherapy cycles (43% versus 47%) in The Netherlands study compared to the current study.

Although a large proportion of elderly patients were able to tolerate and experience a survival benefit from chemotherapy, 48% of patients who began chemotherapy were not able to complete all treatment cycles and did not have a survival benefit. Clearly, all elderly patients are not good candidates for chemotherapy. The difficulty is identifying the ones who are; there is a need for a reliable means to identify elderly patients who would benefit from chemotherapy that does not base its conclusions on chronological age and rather aims to determine biological age by the measurement of objective standard measures [6, 19, 28]. The use of a multidimensional geriatric assessment tool for this purpose has been suggested as a means of achieving this end [19, 29]. Suggested domains of the assessment tool include co-morbidity, functional status, emotional conditions and mental status, social support, polypharmacy, and nutritional state. Even though the tool was first introduced over 15 years ago, the best form of the tool has yet to be defined [6, 29]. Further efforts are needed to optimize such a tool and implement it in routine practice.

A limitation to the study is the nature of all retrospective studies in that they cannot prove causality. Additionally, there is always selection bias in terms of which patients receive treatment in a real clinical situation as opposed to a clinical trial setting. On the other hand, an inherent strength of a population-level retrospective study such as this one is that the treatment and outcome can be described for every

Table 6: Adjusted[1] hazard ratio of death of patients 75 years or older diagnosed with SCLC in 2004–2008 in Alberta, Canada, who had an oncologist-consult[2].

	Adjusted[1] hazard ratio (95% CI)	P value
ECOG Score		$P = 0.02$
0, 1, and 2	1	
3 and 4	2.01 (1.22, 3.31)	0.007
Missing	1.59 (0.88, 2.88)	0.12
Stage		$P = 0.33$
Limited	1	
Extensive	1.24 (0.80, 1.92)	0.33
Age at diagnosis		$P = 0.80$
75–79	1	
≥80	1.06 (0.66, 1.75)	0.80
Co-morbidities		$P = 0.05$
0 or 1	1	
2 or more	1.63 (1.00, 2.66)	0.05
Drug regimen		$P = 0.82$
Cisplatin/etoposide	1	
Carboplatin/etoposide	1.15 (0.5, 2.65)	0.56
Oral etoposide	1.15 (0.71, 1.89)	0.75
Treatment status		$P = 0.0018$
Complete/full dose	1	
Complete/reduced dose	1.02 (0.57, 1.82)	0.94
Not completed	2.72 (1.52, 4.87)	0.0007
No chemotherapy	2.01 (0.97, 4.18)	0.6

[1]Adjusted for all variables shown in the table.
[2]Start time was 12 weeks after the date of the initial oncologist-consult.

patient, as we have done so herein. The major limitations are in obtaining complete information on all the factors that might impact one of or both treatment and outcome in order to properly adjust for them in analyses. In our study we had limited information on the patients who did not have an oncologist-consult, representing 25% of the entire population of SCLC patients aged 75 years or older in Alberta. The data we do have, however, suggests that many of these patients would not have been candidates for any kind of treatment as they died very soon after being diagnosed. It is possible, however, that some of them could have benefited from chemotherapy but did not have the opportunity because they were not referred to an oncologist, were unable to obtain transportation to an oncologist, were not interested in receiving chemotherapy, or another reason. We were not able to identify reasons for not seeing an oncologist. Regarding the patients who did have an oncologist-consult, performance status was missing for 18% of patients, and we did not collect information on receipt of other treatment modalities which could have affected survival and the ability to tolerate chemotherapy. It is possible that there is also missing/incomplete information related to the specific reasons for dose reductions and incomplete cycles. A further limitation arises from the relatively small number of patients with limited disease, which prevented us from fully exploring the interrelationships between age, stage, chemotherapy uptake, tolerance, and survival. Further study in a larger patient population may provide interesting insights on these issues.

5. Conclusion

SCLC is a significant health issue of the elderly. We have shown that while an appreciable proportion of elderly patients diagnosed with SCLC do not begin chemotherapy treatment, those that do are able to tolerate the treatment and receive survival benefits from it. It is, therefore, vital that elderly patients as well as younger patients are considered for established treatment. Our results also suggest that elderly SCLC patients who complete chemotherapy at a reduced dose have a similar prognosis to those who receive the full dose. Future research should focus on better understanding the relationship between frailty and toxicity to ensure the careful selection of patients who will benefit from chemotherapy treatment.

Authors' Contribution

S. Fisher and T. M. Al-Fayea contributed equally to this paper.

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Research Article

Promoting Early Presentation of Breast Cancer in Older Women: Implementing an Evidence-Based Intervention in Routine Clinical Practice

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Background. Women over 70 with breast cancer have poorer one-year survival and present at a more advanced stage than younger women. Promoting early symptomatic presentation in older women may reduce stage cost effectively and is unlikely to lead to overdiagnosis. After examining efficacy in a randomised controlled trial, we piloted a brief health professional-delivered intervention to equip women to present promptly with breast symptoms, as an integral part of the final invited mammogram at age ~70, in the English National Health Service Breast Screening Programme. *Methods*. We trained mammographers, who then offered the intervention to older women in four breast screening services. We examined breast cancer awareness at baseline and one month in women receiving the intervention, and also in a service where the intervention was not offered. *Results*. We trained 27 mammographers to deliver the intervention confidently to a high standard. Breast cancer awareness increased 7-fold at one month in women receiving the intervention compared with 2-fold in the comparison service (odds ratio 15.2, 95% confidence interval 10.0 to 23.2). *Conclusions*. The PEP Intervention can be implemented in routine clinical practice with a potency similar to that achieved in a randomised controlled trial. It has the potential to reduce delay in diagnosis for breast cancer in older women.

1. Introduction

Older women with breast cancer have poorer one-year relative survival than younger women [1] and are more likely to be diagnosed with advanced stage of disease [2]. Older age is a risk factor for delay in presentation in breast cancer [3]. Women over the age of 73 are not routinely invited for screening on the English National Health Service (NHS) Breast Screening Programme; most women with breast cancer of this age group therefore present symptomatically.

We have developed a brief intervention to promote early symptomatic presentation of breast cancer in older women (the Promoting Early Presentation (PEP) Intervention) [4]. It is a scripted one-to-one intervention, delivered to an older woman in a positive, collaborative, and motivational style by a health professional, providing the knowledge, motivation, confidence, and skills to present promptly on discovering a breast symptom. It is supported by a booklet which women are given to take home.

The PEP Intervention increased breast cancer awareness fourfold compared with usual care for up to two years in a randomised controlled trial, in which it was delivered by research health professionals [5, 6], and the effect was sustained after three years (report in preparation). The effect was greater than any other intervention of its kind [7].

The NHS Breast Screening Programme currently invites women aged 50–70 for two-view mammography every three years and a national randomised controlled trial of inviting women aged 47–49 and 71–73 is currently under way. The final invited mammogram provides an opportunity to

promote early presentation to women at increasing risk of developing breast cancer, but no longer routinely invited for screening, at whatever age that may be. By promoting early symptomatic presentation, the PEP Intervention may reduce stage of breast cancer at diagnosis and is unlikely to lead to overdiagnosis: among women aged 70 and over, breast symptoms are very likely to be due to breast cancer [8].

We aimed to examine whether we could train NHS rather than research staff to deliver the PEP Intervention, whether quality of delivery could be maintained, and whether the effect on breast cancer awareness shown in the randomised controlled trial could be replicated in routine clinical practice. We piloted the PEP Intervention, which takes about five minutes, delivered by NHS mammographers as an integral part of the final invited mammogram appointment in four breast screening services.

2. Methods

2.1. Training to Deliver PEP Intervention. During 2011, we offered training to deliver the PEP Intervention to all 63 mammographers (both radiographers and assistant practitioners working in four breast screening services (Cambridge and Huntingdon; Warwickshire, Solihull and Coventry; Maidstone; Medway)). The facilitator-led training involved two half-day group sessions, two to four weeks apart, plus practice sessions with performance feedback in-between provided by coaching radiographers. The training team, including the facilitator and coaching radiographers, assessed competence to deliver the PEP Intervention during and at the end of training by completing a checklist of quality criteria (see the appendix) during observed interventions. The coaching radiographer calculated a quality score for each intervention for content out of 33 and for style out of 6 and converted these to percentages. A satisfactory score was considered to be 70% for content and 50% for style. Having identified strong and weak areas of quality of delivery, the coaching radiographer undertook a performance feedback session with the mammographer. Twelve of the criteria were considered the most important (nine for content and three for style (marked "essential" and "desirable" on the checklist (see the appendix))) and so performance feedback focused mainly on these.

We measured mammographers' confidence to deliver key messages about early presentation before and immediately after training, using a self-complete questionnaire including seven questions answered on a scale of 1–10. We calculated mean scores out of ten for each question before and after training.

2.2. Delivering the PEP Intervention. During the implementation period (between three and six months in each service between May 2011 and February 2012), women attending for final mammogram were allocated longer appointments and offered the PEP Intervention on arrival. The PEP Intervention was delivered as an integral part of the final invited mammogram in the X-ray room.

We implemented a quality assurance programme to ensure consistently high-quality delivery of the PEP Intervention. This involved a coaching radiographer assessing, for each mammographer, an audiotaped intervention every two weeks, and a directly observed intervention every two months, using the checklist of quality criteria (see the appendix). The coaching radiographer assessed quality and used this as the basis for a fifteen-minute performance feedback session as described in the section on training to deliver the PEP Intervention.

2.3. Evaluating the Effect of the PEP Intervention on Breast Cancer Awareness. Evaluating the effect of the PEP Intervention on breast cancer awareness involved the four pilot services and two comparison services which did not offer the PEP Intervention (Norwich and Norfolk and Gateshead Breast Screening Services). Women were sent information about the evaluation with their final invited screening appointment letter three weeks before their appointment. Mammographers invited eligible women to take part when they attended, and if they consented, they were asked to complete a short questionnaire. One month later we sent them the same questionnaire by post.

The questionnaire included a validated measure of breast cancer awareness [9]. This measured knowledge of breast cancer symptoms, knowledge that the risk of breast cancer increases with age and of lifetime risk of breast cancer, reported breast checking, confidence to detect a breast change, and barriers to seeing a doctor with a health problem. Women were also asked to provide ethnic group, whether they lived with a husband or partner and age of leaving full time education. Breast screening services provided date of birth and postcode.

Breast cancer awareness data collection in the pilot services took place over May 2011 to April 2012 and in the comparison services over March 2011 to January 2012. We compared change in breast cancer awareness over one month in women receiving the PEP Intervention in the pilot services with that of women in the comparison services.

We assigned each woman taking part in the evaluation an Index of Multiple Deprivation score (IMD) (2007) based on the area of residence used in the Census 2001 (higher scores indicate more socioeconomic deprivation: the IMD summarises income, employment, health and disability, education and skills, housing, service access, living environment, and experience of crime, based on a range of routine data sources, for a geographical area). We examined demographic differences between women who received the PEP Intervention and women in the comparison services and between women who responded at one month and women who responded at baseline only.

Women were considered breast cancer aware if they knew that risk of breast cancer increased with age, recognised five or more nonlump symptoms of breast cancer, and reported checking their breasts at least once a month.

We used repeated measures logistic regression models to examine change in breast cancer awareness from baseline to one month comparing women who received the PEP Intervention with women in the comparison services, including only those who provided data at both time points. We examined the effect on the odds ratios of controlling for demographic differences between the groups.

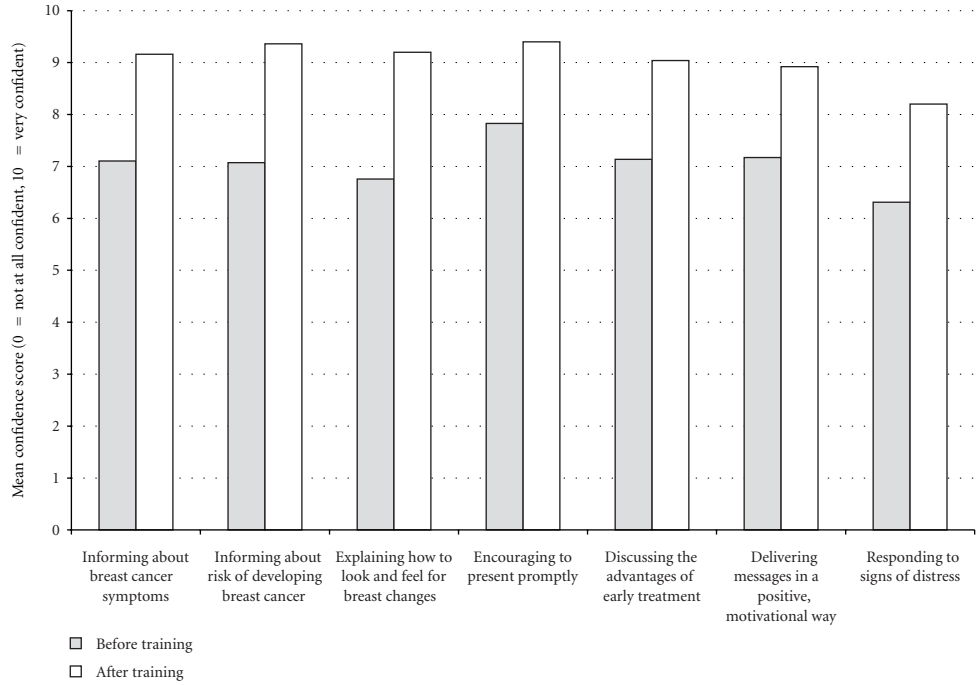

Figure 1: Mammographers' mean confidence scores before and after training.

We carried out semistructured interviews with mammographers several weeks after training to gain their impressions of training, coaching, performance feedback and delivery of the intervention, and how they felt it had contributed to their professional development.

The project received ethics approval from the Cambridgeshire 1 Research Ethics Committee (10/H0304/90).

3. Results

Thirty two mammographers started and 27 completed the training programme (five did not complete it because of health problems and family commitments). At the end of training, all 27 were delivering the PEP Intervention to a satisfactory level (70% or more for content and 50% or more for style). Mean confidence scores for all seven questions increased over the training period (Figure 1).

Eight hundred and thirty women were offered the PEP Intervention (25% of women attending for their final invited mammogram at the four services) and 551 (66%) took it up. Nineteen mammographers ultimately delivered these interventions—eight were not able to for a variety of personal and service reasons. Quality of delivery was well maintained for these 19 mammographers: based on fortnightly assessments, mean scores for content never fell below 80% and mean scores for style never fell below 70%.

In the pilot services, 511 women were asked to participate in the evaluation of breast cancer awareness; 495 (97%) agreed to take part and completed a baseline questionnaire. Four hundred and fifty seven (92%) women also completed the one-month questionnaire. In one of the comparison services, 880 (64%) women attending for final invited mammogram agreed to take part and completed the baseline questionnaire; 789 (90%) women also completed the one-month questionnaire. In the other comparison service, only 82 (36%) women attending for their final invited mammogram agreed to take part and completed the baseline questionnaire. This is likely to have been because mammographers found it difficult to recruit women due to ongoing service developments, in particular the introduction of digital mammography. We did not include the women attending this service in the analysis because of the low response rate.

Women who responded at both time points were more likely to be White and slightly less likely to live in socioeconomically deprived areas than women who responded at baseline only (White: 98% versus 94%, $P < 0.001$; median IMD 11.1 versus 12.0, $P = 0.03$).

Table 1 shows the demographic characteristics of participating women. Most were White and lived with a husband or partner. Women who received the PEP Intervention were slightly older, less likely to be living with a husband or partner, more likely to have left school after the age of 18, and less likely to be living in socioeconomically deprived areas than women in the comparison service.

Table 2 shows change in breast cancer awareness and confidence to notice a breast change in the women who received the PEP Intervention and the women in the comparison service. Women who received the PEP Intervention had a much greater increase in breast cancer awareness than the comparison group. The increase was seen for all components of the score: women who received the PEP Intervention were more likely to recognise five or more nonlump symptoms of breast cancer, to know that a 70-year-old woman was most at risk of breast cancer compared to a 30- or 50-year-old

Table 1: Characteristics of women participating in the evaluation.

	Women in comparison service $n = 875$	Women receiving PEP Intervention $n = 495$	
Mean age	68 years, 9 months	71 years, 4 months	$P < 0.001$
Living with husband or partner	670 (76.6%)	340 (68.7%)	$P < 0.001$
Left full time education aged 19 or older	88 (10.1%)	109 (22.0%)	$P < 0.001$
White ethnic group	854 (97.6%)	484 (97.8%)	$P = 0.42$
Median Index of Multiple Deprivation	11.39	8.12	$P < 0.001$

Table 2: Change in breast cancer awareness and confidence to notice a breast change.

	Comparison service ($n = 789$)		PEP Intervention ($n = 457$)		Crude odds ratio (95% confidence interval)
	Baseline	One month	Baseline	One month	
Breast cancer aware	24 (2.9%)	30 (3.9%)	19 (4.2%)	167 (37.7%)	15.24 (10.0 to 23.2)
Knew five or more nonlump symptoms	457 (52.2%)	461 (59.3%)	244 (52.8%)	373 (82.5%)	3.26 (2.48 to 4.30)
Knew that risk of breast cancer increases with age	70 (8.2%)	59 (7.6%)	66 (13.3%)	247 (49.9%)	15.39 (11.1 to 21.35)
Reported checking breasts at least once a month	494 (57.0%)	506 (64.5%)	249 (50.3%)	359 (78.7%)	2.10 (1.61 to 2.73)
Knew lifetime risk of breast cancer (1 in 8)	419 (49.2%)	372 (47.8%)	244 (50.2%)	272 (60.4%)	1.67 (1.32 to 2.10)
"Fairly" or "very" confident to notice change in breasts	603 (69.6%)	619 (78.8%)	348 (70.7%)	391 (85.6%)	1.61 (1.19 to 2.19)

woman or a woman of any age and more likely to report checking their breasts at least once a month than women in the comparison service after one month. Women who received the PEP Intervention were also more likely to know the lifetime risk of breast cancer and to report being "fairly" or "very confident" that they would notice a change in their breasts at one month compared with the comparison service. Adjusting for age, living with a husband or partner, age left full time education, and IMD made little difference to the odds ratios.

Barriers to symptomatic presentation were relatively rarely reported by the women (Table 3). The most frequently reported issues making it difficult to see a doctor with a health problem were feeling that they were bothering their doctor, finding it difficult to make an appointment and worrying that the doctor is too busy to listen to them. The PEP Intervention had limited influence on barriers; the only statistically significant differences were very small: women who received the PEP Intervention were less likely to report that finding it difficult to make an appointment, that the doctor was too busy to listen to them, and that it was physically difficult to get to the surgery than in the comparison group. Adjusting for age, living with a husband or partner, age left full time education, and IMD made little difference to the odds ratios.

In interviews, mammographers were very positive about training, coaching, performance feedback, and delivery of the PEP Intervention. They saw the PEP Intervention as extending their role, enhancing their professional development, and they particularly valued the opportunity it gave them to interact with their clients.

4. Discussion

We successfully piloted implementation of the PEP Intervention in four breast screening services: we trained NHS mammographers who delivered the intervention confidently to a high standard, and who were positive about its effect on their professional development. Uptake of the intervention was good. The intervention increased breast cancer awareness at one month from 4% at baseline to 38% at one month. The effect of the intervention on breast cancer awareness in routine clinical practice is of a similar size as achieved by the PEP Intervention delivered within the randomised controlled trial, which increased breast cancer awareness at one month from 2% at baseline to 33% at one month [6]. The PEP intervention had large effects on all the aspects of breast cancer awareness. It had a more limited effect on reported barriers to symptomatic presentation.

Our study shows that the PEP Intervention is as potent after one month when delivered in routine clinical practice by NHS staff as when delivered by research radiographers with very close quality control in a randomised controlled trial. We were surprised at this finding: interventions, whether pharmacological or complex, are often less potent in routine clinical practice than in randomised controlled trials [10–12]. There are many possible reasons for this, including that in randomised controlled trials the delivery of the intervention being tested is strictly controlled, and the participants are self-selected and more motivated with better potential for a positive outcome [13]. The success of the PEP Intervention in routine clinical practice is likely to be due to a high level of mammographer motivation engendered by

Table 3: Change in reported barriers to seeing a doctor with a health problem.

	Comparison service ($n = 789$)		PEP Intervention ($n = 457$)		Crude odds ratio (95% confidence interval)
	Baseline	One month	Baseline	One month	
I feel that I am bothering my doctor	74 (8.6%)	89 (11.3%)	63 (12.8%)	50 (11.0%)	0.95 (0.66 to 1.37)
It is usually difficult for me to get an appointment	67 (7.7%)	99 (12.6%)	32 (6.5%)	30 (6.6%)	0.48 (0.32 to 0.74)
I worry that he/she is too busy to listen to me	38 (4.4%)	61 (7.8%)	25 (5.1%)	21 (4.6%)	0.59 (0.35 to 0.98)
I worry about any treatment I might have to have	27 (3.1%)	43 (5.5%)	28 (5.7%)	24 (5.3%)	0.95 (0.57 to 1.59)
I feel embarrassed to go to my doctor in case he/she has to examine me	18 (2.1%)	19 (2.4%)	8 (1.6%)	13 (2.9%)	1.18 (0.57 to 2.43)
I have other more important things to think about or do	17 (2.0%)	23 (2.9%)	16 (3.3%)	15 (3.3%)	1.15 (0.60 to 2.18)
It is physically difficult for me to get to the surgery	10 (1.2%)	13 (1.7%)	3 (0.6%)	1 (0.2%)	0.18 (0.03-0.96)

the training and coaching, and attributes of the intervention itself, which gives the mammographers an opportunity to communicate positively with their clients.

We found that the PEP Intervention had little effect on reported barriers to symptomatic presentation. This may be at least partly because barriers were rarely reported by the women. We note that the commonest barrier to early presentation reported was "I feel I am bothering my doctor," reported by about 11% of women. This is less than has been found in other studies of barriers to symptomatic presentation asking a similar question, which have found that over 30% of British people reported that worry about wasting the doctor's time might put them off seeing a doctor with a symptom that might be serious [14, 15].

Our evaluation of the pilot implementation of the PEP Intervention was not as methodologically robust as the randomised controlled trial: in the pilot, women were not randomly allocated to receive the intervention or not, so those receiving the intervention may have differed in many ways from those who did not, in the comparison services. However, adjusting for known differences between the women in the intervention and comparison services made little difference to the findings. Moreover, the effect size was so large that variation in outcome between the intervention and comparison services is unlikely to be due simply differences between the populations involved.

Implementation was not complete: the services did not manage to offer the PEP Intervention to all women attending for final mammogram. This was because not all mammographers were trained to deliver the intervention, and implementation was limited by the capacity of existing clinics and availability of temporary staff to backfill the trained mammographers' time. Were the intervention to be implemented more widely, it would be necessary to expand capacity of the services to incorporate an extra five minutes for every woman attending for their final invited mammogram (about 1 in 7 mammograms delivered).

Uptake of the intervention among women was good, suggesting that the intervention was an acceptable part of the mammogram appointment.

Whether increasing breast cancer awareness will reduce breast cancer mortality is not yet known. The evaluation is ongoing and will, in due course, report the effect on breast cancer awareness at one year, self-referral for screening, symptomatic breast clinic attendances, and breast cancer mortality. There is indirect evidence that breast cancer awareness influences mortality: women who delay presentation in breast cancer are more likely to have poor awareness of symptoms [3], and delay in diagnosis is related to worse survival in breast cancer [16].

The UK has worse breast cancer survival than many countries with good access to high-quality health care [17]. We estimate that 7,000–12,000 women in England delay presentation for >3 months each year [16, 18]. These women have 7% lower 5-year survival than those with shorter delays [16]. This suggests that at least 500 women in England will die because of delayed presentation each year (assuming a 5-year breast cancer survival of 80% in women who delay <3 months and 73% in those who delay >3 months). Delivered to all women attending for their final invited mammogram on the NHS Breast Screening Programme, at whatever age that may be, the PEP Intervention could contribute to improving cancer survival in England so that it is nearer to that achieved in similar countries.

Appendix

For quality criteria to assess mammographers' competence to deliver the intervention see Supplementary Material available online at doi:10.1155/2012/835167.

Conflict of Interests

The authors declare that they have no conflict of interests.

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Clinical Study

Chronic Diseases among Older Cancer Survivors

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Objective. To compare the occurrence of pre-existing and subsequent comorbidity among older cancer patients (≥ 60 years) with older non-cancer patients. *Material and Methods*. Each cancer patient ($n = 3835$, mean age 72) was matched with four non-cancer patients in terms of age, sex, and practice. The occurrence of chronic diseases was assessed cross-sectionally (lifetime prevalence at time of diagnosis) and longitudinally (incidence after diagnosis) for all cancer patients and for breast, prostate, and colorectal cancer patients separately. Cancer and non-cancer patients were compared using logistic and Cox regression analysis. *Results*. The occurrence of the most common pre-existing and incident chronic diseases was largely similar in cancer and non-cancer patients, except for pre-existing COPD (OR 1.21, 95% CI 1.06–1.37) and subsequent venous thrombosis in the first two years after cancer diagnosis (HR 4.20, 95% CI 2.74–6.44), which were significantly more frequent ($P < 0.01$) among older cancer compared to non-cancer patients. *Conclusion*. The frequency of multimorbidity in older cancer patients is high. However, apart from COPD and venous thrombosis, the incidence of chronic diseases in older cancer patients is similar compared to non-cancer patients of the same age, sex, and practice.

1. Introduction

With advances in early detection and cancer treatments, numbers of cancer survivors are rising [1], and with the ageing of the population, the number of older cancer survivors will continue to rise even if age-specific incidence rates remain constant [2]. Whereas cancer used to be a fatal disease, it is now developing towards a chronic or even curable disease [3, 4]. At present, more than 60% of older cancer patients suffer from one or more chronic diseases [5]. Because of the chronic character of cancer [6] and the high level of comorbidity [7], the role of general practitioners (GPs) in cancer aftercare will become more prominent [7, 8].

Studies among cancer survivors have shown that the consequences of cancer treatment are numerous and depend on the type of cancer and treatment characteristics [4, 9]. The most common sequelae are second malignancies (due to genetic or environmental risk factors shared with the first tumour and treatment-related factors) and cardiovascular diseases as myocardial infarction and cardiac insufficiency (due to radiotherapy as well as chemotherapy) [9]. Many other diseases, such as osteoporosis [10] and diabetes [11], have been related to cancer treatment also. These late effects are also common ageing-related diseases. Therefore, within primary care, which is characterized by a heterogeneous patient population and "only" 50 cancer patients per standard practice (of 2350 patients) [12], the late effects of cancer and its treatment could easily be mistaken for normal ageing and dismissed as such in older cancer survivors [13]. Given the GPs' expertise in dealing with multimorbidity, we believe that GPs could play an important role in aftercare for cancer survivors. Hence, primary care providers are in urgent need of more knowledge on the interaction between cancer, cancer treatment, and comorbidity in older cancer patients.

Therefore, we aim to examine from a generic GP perspective the occurrence of pre-existing (prevalent) and subsequent (incident) chronic diseases among cancer patients aged over 60, in comparison with non-cancer patients of the same age, sex, and practice in a large retrospective primary care-based cohort study.

2. Materials and Methods

2.1. The Registration Network Family Practices. This study was carried out within the context of the Registration Network Family Practices (RegistratieNet Huisartspraktijken, RNH) [14]. This is a continuously updated computerized primary care database, with a target population of about 135,000 people. All relevant health problems are routinely recorded using a computerized health information system. All participants were informed about the anonymous use of information about their health status when they registered as patients with the participating general practices (21 participating practices and about 65 general practitioners).

All relevant health problems—current as well as past—are recorded on a problem list. A health problem is defined as "anything that has required, does or may require health care management and has affected or could significantly affect a persons' physical or emotional well-being." Health problems are coded using the International Classification of Primary Care (ICPC), following the criteria of the International Classification of Health Problems in Primary Care (ICHPPC-2-defined) for diagnoses [14]. In the Netherlands, GPs have comprehensive information on the health status of their patients because GPs function as gatekeepers to other health care facilities, and it is compulsory for all Dutch residents to have health care insurance and to register with a GP. Hence, we can expect the registered population to be representative of the general population. In addition to medical information, the RNH database also contains background information on sex, date of birth, living arrangement, level of education, and the date and reason of removal. RNH registration only ends upon migration or death. The quality of the data is assured by instruction and training sessions, regional consensus groups, quality control experiments, and special software programs, such as an automated thesaurus and automated checking for erroneous or missing entries [14]. Reliability and completeness have been proved previously [15].

2.2. Design and Data Analysis. The design of this study is a retrospective cohort, including all patients who were members of the RNH database between 1 January 1998 and 31 December 2010, and aged 60 years and over. Patients with a previous cancer history (diagnosed before January 1998) were excluded. Neoplasms of the skin were excluded as well, as due to the ICPC coding we were unable to distinguish between benign and malign neoplasma of the skin. Each cancer patient, diagnosed between January 1998 and December 2010 ($n = 3835$), was matched with four non-cancer patients based on age, sex, and practice. For 239 cancer patients, we were unable to find an appropriate match. 337, 428, 429, and 3596 cancer patients were matched with one, two, three, and four non-cancer patients respectively. Matched non-cancer patients were assigned a reference date (the same as the date of the cancer diagnosis of their matched cancer patient).

Only ICPC codes that correspond to severe or chronic diseases were selected and categorized as previously described by Knottnerus et al. [16] (please see Table 1 in the Supplementary Material available online at doi:10.1155/-2012/206414).

Pre-existing chronic diseases were defined as all diagnoses established before the cancer diagnosis or reference date. Subsequent chronic diseases were defined as all diagnoses established after the cancer diagnosis or reference date. All diagnoses that were established within a 3-month period before removal from the RNH database were excluded, as these might reflect the palliative phase, in which the disease pattern might be different. Pre-existing chronic diseases were assessed by calculating the lifetime prevalence (per 1000 persons) cross-sectionally at the time of the cancer diagnosis or the reference date and were compared between cancer patients and their matched non-cancer patients using logistic regression analyses, adjusted for age and sex. Prevalence and odds ratios were calculated for all cancer patients together, and for breast, prostate, and colorectal cancer patients separately. The occurrence of subsequent chronic diseases was longitudinally assessed by calculating the incidence per 1000 person-years at risk, excluding patients with a previous diagnosis of the disease. Hazard ratios and their 95% confidence intervals (95% CIs) were calculated using multivariate Cox regression analyses, adjusted for age, sex, and presence of cardiovascular diseases, respiratory diseases, or diabetes at baseline (please see Table 1 in the Supplementary Material on the journal website for the precise cardiovascular and respiratory diseases which were included). Incidence and hazard ratios were computed for all cancer patients in comparison with their age, sex, and practice-matched controls and for all breast, prostate, and colorectal cancer patients separately, in comparison with their respective matched controls. The proportional hazards assumption was tested using Schoenfeld residuals. For venous thrombosis (K93+K94), limited mental function (P28), lipid disorders (T93), and other endocrine/metabolic/nutritional diseases (T99), proportional hazards assumption was violated. This was resolved by splitting the survival time.

Analyses were processed with the STATA statistical software package (StataCorp. 2009. Stata: Release 11. Statistical Software. College Station, TX: StataCorp LP). Throughout all analyses, a two-sided P-value <0.01 was used as the cut-off point for statistical significance.

3. Results

3.1. Population. In the thirteen-year study period (1998–2010), there were 3,835 patients with a first diagnosis of cancer who were 60 years or older at the time of their cancer diagnosis (see Table 1). These cases were matched to 11,973 controls.

Table 1: Characteristics of older cancer patients and non-cancer patients at time of cancer diagnosis or reference date.

	Cancer patients (N = 3835)		Non-cancer patients (N = 11973)	
	Mean	(SD)	Mean	(SD)
Age (years)				
Men	71.95	(7.35)	70.87	(7.13)
Women	73.22	(8.42)	72.90	(8.27)
Survival time (years)[1]				
Men	2.92	(3.06)	3.87	(3.15)
Women	3.32	(3.39)	4.17	(3.27)
	N	(%)	N	(%)
Sex				
Men	2163	(56)	6179	(52)
Women	1672	(44)	5794	(48)
Number of chronic diseases at baseline[2]				
0	846	(22)	2617	(22)
1	908	(24)	2916	(24)
2	752	(20)	2288	(19)
3	534	(14)	1682	(14)
≥4	795	(21)	2470	(21)
Five most common tumour sites				
Colon/rectum	675	(18)		
Prostate	573	(15)		
Bronchus/lung	550	(14)		
Breast	493	(13)		
Bladder	218	(7)		

[1] Survival time: time from date of diagnosis or reference date until death or end of follow-up.
[2] Number of chronic diseases excluding cancer.

3.2. Pre-Existing Chronic Diseases. The prevalence of pre-existing chronic diseases was high; 78% of all cancer patients had at least one disease additional to the malignancy at time of cancer diagnosis (see Table 1).

The most common pre-existing chronic diseases were the same for cancer patients and non-cancer patients. These were diabetes, lipid disorders, ischemic heart disease, myocardial infarction, and COPD. COPD was significantly more prevalent among cancer patients compared to non-cancer patients (OR 1.21, 95% CI 1.06–1.37). Furthermore, dementia (OR 0.48, 95% CI 0.36–0.64) and personality disorder (OR 0.53, 95% CI 0.33–0.84) were significantly less prevalent in cancer patients compared to non-cancer patients (see Table 2).

When stratified by cancer type (data not shown), we found no differences within breast cancer patients (n = 493) compared to their matched controls (n = 1675). For prostate cancer patients (n = 573) compared to their respective controls (n = 1604), we found a higher prevalence of benign prostatic hypertrophy (OR 1.44, 95% CI 1.09–1.88) and a lower prevalence of stroke (OR 0.40, 95% CI 0.25–0.65) and diabetes (OR 0.67, 95% CI 0.51–0.90). For colorectal cancer patients (n = 675) in comparison with their controls (n = 2063), we found a higher prevalence of blindness (OR 2.85, 95% CI 1.43–5.71) and a lower prevalence of stroke (OR 0.60, 95% CI 0.41–0.89), dementia (OR 0.26, 95% CI 0.12–0.56), and benign prostatic hypertrophy (OR 0.55, 95% CI 0.36–0.83).

3.3. Subsequent Chronic Diseases. Just as for pre-existing chronic diseases, risk of subsequent chronic diseases was similar among cancer survivors and non-cancer patients. The most common incident diseases in cancer patients were diabetes, venous thrombosis, osteoporosis, COPD, and heart failure. In non-cancer patients these were diabetes, benign prostatic hypertrophy, stroke, dementia, and COPD. In cancer survivors, the incidence of subsequent venous thrombosis was significantly higher compared to non-cancer patients during the first two years of survival (HR 4.20, 95% CI 2.74–6.44). Thereafter, this difference was no longer statistically significant (see Table 3). Furthermore, the incidence of hypertension with organ damage (HR 0.66, 95% CI 0.48–0.92), lipid disorders during the first two years after diagnosis (HR 0.49, 95% CI 0.29–0.82), and benign prostatic hypertrophy (HR 0.46, 95% CI 0.31–0.69) was significantly lower in cancer patients compared to non-cancer patients (see Table 3).

When stratified by cancer type (data not shown), we found no differences for breast cancer patients compared to their respective controls. In prostate cancer patients, the incidence of venous thrombosis (HR 7.10, 95% CI 2.25–22.40) was significantly higher compared to non-cancer patients, and the incidence of benign prostatic hypertrophy was significantly lower (HR 0.17, 95% CI 0.06–0.48). In colorectal cancer patients, the incidence of venous thrombosis (HR 2.43, 95% CI 1.22–4.81) was significantly higher compared to non-cancer patients.

4. Discussion

4.1. Principal Findings. The number of chronic diseases additional to cancer proved to be high and is probably associated with high age in the first place. Both prevalence at diagnosis and incidence, however, tend to be largely similar in older cancer and non-cancer patients. The latter is consistent with recent other studies [17, 18].

4.2. Pre-Existing Chronic Diseases. At time of cancer diagnosis, 78% of all cancer patients had at least one disease additional to the malignancy. This highlights the enormous burden of comorbidity in older cancer patients. However, from the perspective of a GP, it is also important that cancer and non-cancer patients were similar with respect to prevalence of chronic diseases. Still, there were some exceptions. In cancer patients, the prevalence of COPD was significantly higher compared to non-cancer patients. When stratified by cancer type, this difference remained significant, only within the group of lung cancer patients (OR 2.88, 95% CI 2.20–3.78) (data not shown). This is in line with previous reports [19] and is probably due to shared risk factors such as smoking [20]. Based on previous studies on the interaction between cancer and comorbidity, we would have expected an

Table 2: Pre-existing chronic diseases in men and women.

	Cancer patients		Non-cancer patients		P-value	OR[2]	(95% CI)
	N	Prev[1]	N	Prev[1]			
Ten most common pre-existing diseases in cancer patients							
Diabetes mellitus	586	152.80	1864	155.68	0.48	0.96	(0.87–1.07)
Lipid disorders	508	132.46	1559	130.21	0.60	1.03	(0.92–1.15)
Ischemic heart disease with angina	459	119.69	1326	110.75	0.73	1.02	(0.91–1.14)
Myocardial infarction	405	105.61	1162	97.05	0.86	1.01	(0.90–1.14)
Ischemic heart disease without angina	393	102.48	1151	96.13	0.98	1.00	(0.88–1.13)
Chronic obstructive pulmonary disease	382	99.61	944	78.84	**0.00**	**1.21**	**(1.06–1.37)**
Osteoarthrosis knee	312	81.36	1054	88.03	0.17	0.91	(0.80–1.04)
Benign prostatic hypertrophy	297	77.44	740	61.81	0.33	1.08	(0.93–1.25)
Back syndrome without radiating pain	281	73.27	888	74.17	0.70	0.97	(0.85–1.12)
Osteoarthrosis hip	272	70.93	885	73.92	0.47	0.95	(0.82–1.09)
Significant differences between cancer and non-cancer patients[3]							
Dementia	60	15.65	344	28.73	**0.00**	**0.48**	**(0.36–0.64)**
Personality disorder	21	5.48	127	10.61	**0.01**	**0.53**	**(0.33–0.84)**

[1] Prev: lifetime prevalence per 1000 persons.
[2] OR: odds ratio adjusted for sex and age.
[3] Please see Table 2 in the Supplementary Material on the journal website for all other diseases.

Table 3: Subsequent chronic diseases in men and women.

	Cancer survivors		Non-cancer patients		P-value	HR[2]	(95% CI)	
	N	Inc[1]	N	Inc[1]				
Ten most common subsequent diseases in cancer patients								
Diabetes mellitus[†]	133	13.46	589	14.79	0.31	0.91	0.75	1.09
Venous thrombosis								
Baseline—2 years	45	9.27	40	2.11	**0.00**	**4.20**	**2.74**	**6.44**
2 years—end of follow-up[†]	20	3.10	58	2.11	0.15	1.45	0.87	2.41
Osteoporosis	99	8.93	354	7.90	0.15	1.18	0.94	1.47
Chronic obstructive pulmonary disease	95	8.81	378	8.56	0.97	1.00	0.80	1.25
Heart failure[δ]	94	8.31	380	8.28	0.80	0.97	0.77	1.22
Stroke/cerebrovascular accident	92	8.27	435	9.81	0.08	0.82	0.65	1.03
Dementia[β]	83	7.16	417	8.93	0.07	0.81	0.64	1.02
Ischemic heart disease without angina[β]	71	6.76	308	7.17	0.50	0.92	0.71	1.19
Ischemic heart disease with angina	65	6.29	294	7.03	0.36	0.88	0.67	1.15
Osteoarthrosis hip	66	6.05	268	6.11	0.95	1.01	0.77	1.32
Significant differences between cancer and non-cancer patients[3]								
Hypertension with organ damage	41	3.67	250	5.55	**0.01**	**0.66**	**0.48**	**0.92**
Lipid disorders								
Baseline—2 years	16	3.66	129	7.62	**0.01**	**0.49**	**0.29**	**0.82**
2 years—end of follow-up	31	5.27	171	7.08	0.16	0.76	0.52	1.11
Benign prostatic hypertrophy	27	5.05	223	10.87	**0.00**	**0.46**	**0.31**	**0.69**

[1] Inc: incidence per 1000 person years at risk.
[2] HR: hazard ratio adjusted for sex, age, cardiovascular diseases, respiratory diseases, and diabetes.
[3] Please see Table 3 in the Supplementary Material on the journal website for all other diseases.
[†] Adjusted for age as time-varying coefficient.
[δ] Adjusted for sex and age as time-varying coefficient.
[β] Adjusted for cardiovascular diseases as time-varying coefficient.

increased prevalence of diabetes in colorectal cancer patients [21]. The point estimator was higher than one, but the absolute difference was small and not statistically significant.

We found a significant lower prevalence of dementia in cancer patients compared to non-cancer patients. This has been previously reported and is also known as inverse cancer comorbidity [22]. Probably, malignancies are not less frequently occurring, but less frequently diagnosed in patients with dementia. In line with Tabarés-Seisdedos et al., we also found inverse comorbidity for diabetes in prostate cancer patients [22], which may be related to diabetes treatment [23, 24]. Furthermore, we showed inverse comorbidity for stroke in both prostate and colorectal cancer patients. A negative association between prostate and colorectal cancer and stroke was also shown by others [17], however, a clear explanation is still lacking [25]. In this perspective Tabarés-Seisdedos et al. stated that "further research is needed as analyses of inverse cancer comorbidity can help us understand why some people are protected from certain cancers, and might help to uncover the mechanisms underlying malignancy" [22].

4.3. Subsequent Chronic Diseases. After cancer diagnosis we showed similar to pre-existing diseases that the most common new diseases in cancer survivors were also the most common ones in non-cancer survivors. In line, a recent and similar study by Khan et al. showed that long-term cancer survivors are a population at risk but that the absolute increase in disease burden is small [26].

For venous thrombosis we showed a significantly increased hazard ratio during the first two years of survival. This is in line with previous studies on consequences of cancer treatment [27] and was also confirmed for breast (P-value 0.03), prostate (P-value 0.00), and colorectal (P-value 0.01) cancer patients separately. Therefore, GPs should be alert for the occurrence of venous thrombosis in older cancer survivors, especially within the first two years after diagnosis.

Although it is not the scope of this study, we were unable to confirm a higher incidence of osteoporosis (due to hormone replacement therapy), hypothyroidism (due to radiotherapy), and heart failure (due to radiotherapy and chemotherapy) in specific groups of cancer survivors compared to non-cancer survivors [26]. This may result from small absolute differences and a lower power of our study. Furthermore, the time frame of our study does not enable us to study the occurrence of late effects of cancer therapy. As described by Hewitt et al. "late effects appear months to years after the completion of therapy" [4]. However, we continue our followup of the included patients and hope to come forward with late effect results at a later time.

Besides the increased risk for venous thrombosis, we found a lower incidence of hypertension with organ damage and lipid disorders (only during the first two years after cancer diagnosis) in cancer patients compared to non-cancer patients. In the first period after diagnosis, a decrease in food intake due to side effects of treatment and emotional factors, and later increased surveillance, and attention for healthy lifestyle might explain this lower incidence. A recent study showed, however, no obvious difference in lifestyle factors among short- and long-term cancer survivors compared to controls [28]. Furthermore, data on hyperlipidemia have been previously shown to be heterogeneous [21]. We also found a significant lower incidence of benign prostatic hypertrophy in all cancer patients compared to non-cancer patients. As expected, when stratified by cancer type, this difference only remained for prostate and bladder cancer patients (data not shown).

4.4. Strengths and Limitations. An important strength of this study was that the comprehensive registration of diseases was based on GPs' daily practice and that this data was analysed in a retrospective cohort design.

A shortcoming of this study was that information on cancer treatment and smoking status was incomplete. Therefore we were unable to analyse the risk of comorbidity according to treatment type and to consider smoking as a confounder. This is an important drawback because late effects in cancer survivors are treatment specific [4]. However, to assess the consequences of cancer treatment as such was beyond the scope of this study. The aim of this study was to assess the frequency of comorbidity in cancer patients from a GP perspective, who sees only a small number of cancer patients (about 50 per standard practice) with very diverse cancer types. Hence, we aimed to assess in a generic way the disease burden in older cancer patients, and we aimed to assess whether these cancer patients present to their GP with different diseases compared to non-cancer patients of the same age, sex, and practice.

Another limitation was that some associations may have occurred by chance (Type I error) due to multiple comparisons. The chance of Type I errors can be diminished by applying a Bonferroni correction. However, this would dramatically increase the chance for Type II errors. According to Rothman it is not necessary to correct for multiple comparisons as the underlying premise of research is that nature follows regular laws that may be studied through observation [29, 30]. Therefore, we decided not to formally correct for multiple comparisons and to use a P-value of 0.01 as cut-off for statistical significance. This does, however, not prohibit that some findings might have occurred due to chance, such as the increased prevalence of blindness, and the decreased prevalence of prostatic hypertrophy in colorectal cancer patients, and personality disorders in cancer patients in general. Furthermore, we showed that prostatic hypertrophy was more prevalent in prostate cancer patients, which is probably due to indication bias. Therefore, it is important that these results are validated in similar cohorts.

Because of the similarities between older cancer and non-cancer patients and the GPs' expertise in dealing with multimorbidity, we believe that GPs could play an important role in aftercare for cancer survivors. However, the participation of primary care in cancer care is still in its infancy. Hence, further research is needed. Future studies could focus on the coordination of aftercare between primary and secondary care, the development of guidelines for cancer

patients with comorbidity, and the use of patient goals in the determination of care planning in patients with complex care needs.

Conflict of Interests

The authors declared no conflict of interests.

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Clinical Study

Double Jeopardy? Age, Race, and HRQOL in Older Adults with Cancer

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Understanding the post-treatment physical and mental function of older adults from ethnic/racial minority backgrounds with cancer is a critical step to determine the services required to serve this growing population. The double jeopardy hypothesis suggests being a minority and old could have compounding effects on health. This population-based study examined the physical and mental function of older adults by age (mean age = 75.7, SD = 6.1), ethnicity/race, and cancer (breast, prostate, colorectal, and gynecologic) as well as interaction effects between age, ethnicity/race and HRQOL. There was evidence of a significant age by ethnicity/race interaction in physical function for breast, prostate and all sites combined, but the interaction became non-significant (for breast and all sites combined) when comorbidity was entered into the model. The interaction persisted in the prostate cancer group after controlling for comorbidity, such that African Americans and Asian Americans in the 75–79 age group report lower physical health than non-Hispanic Whites and Hispanic Whites in this age group. The presence of double jeopardy in the breast and all sites combined group can be explained by a differential comorbid burden among the older (75–79) minority group, but the interaction found in prostate cancer survivors does not reflect this differential comorbid burden.

1. Introduction

By 2030, nearly one in five US residents will be >65 years of age and this group is projected to reach 72 million by that year, a doubling of the number in 2008 [1]. During this period, it is estimated that the percentage of all cancers diagnosed in older adults and ethnic/racial minorities will increase from 61% to 70% and from 21% to 28%, respectively [2]. Historically, older adults and minorities have been underrepresented in cancer clinical trials which can ultimately lead to disparities in treatment and outcomes. An important outcome that has received little attention is the posttreatment health-related quality of life (HRQOL) of older adults with cancer from minority backgrounds. The double jeopardy hypothesis suggests that being a minority and old could have additive negative effects on health outcomes [3–5]. Understanding the post-treatment burden of older adults and minorities with cancer is a critical step to determine the services and resources required to serve this rapidly growing population.

While the long-term surveillance of older adults and minorities with cancer is limited, evidence suggests physical and social functioning are the most common HRQOL domains affected by cancer and its treatment, with mixed findings for mental health for this group of survivors [6–12]. A population-based study of 703 adult breast cancer survivors found significant ethnic differences in HRQOL, with Latinos reporting greater role limitations and lower

emotional well-being than Caucasians, African Americans, and Asian Americans [11]. Another study, focused on disparities in older cancer survivors and non-cancer-managed care enrollees, found physical and mental function were lower in Hispanic cancer survivors compared with Caucasian and African Americans [8]. Deimling and colleagues found older, African American cancer survivors experience poorer functional health and higher levels of comorbidity and decreased physical functioning after cancer compared with older Caucasian cancer survivors [7]. Most recently, a prospective study of 1,432 older cancer survivors and 7,160 matched controls found significant declines in physical function and mental health across several cancer sites relative to the mean change of the control group [13]. Despite the contribution of these few studies to our understanding of HRQOL in older adults from minority backgrounds, they are mostly confined to survivors of prostate or breast cancer or are restricted to short-term (i.e., less than 5 years) survivors. Importantly, studies that have examined the effect of age and race have done so in isolation without attention to possible interaction effects between these important, yet understudied correlates of HRQOL. Other factors found to be related to quality of life in cancer survivors, including optimism, perceived control, and social support were also examined to control for these effects on HRQOL outcomes [9, 11].

To examine the relationship between age and race/ethnicity with HRQOL among cancer survivors, we conducted one of the largest population-based studies of long-term, ethnically diverse, adult cancer survivors in the United States. The overall goal of the study was to obtain information regarding medical follow-up care and late health effects, including HRQOL during the extended survivorship years to facilitate the development of standards or best practices for such care. The specific objectives of these analyses were: (1) to examine the HRQOL of older long-term cancer survivors by cancer type (breast, prostate, colorectal, and gynecologic cancer), ethnicity/race (non-Hispanic White, Hispanic White, African American and Asian American) and age group (65–74, 75–84 and 85 plus) and (2) to examine potential interaction effects between age and ethnicity/race as well as other demographic, health, and psychosocial correlates of HRQOL in older long-term cancer survivors. We hypothesized that there would be a significant interaction effect between minority status and age, with ethnic/racial minority disparities in HRQOL increasing with age.

2. Methods

2.1. Participants and Procedures. Study subjects were men and women who participated in the Follow-Up Care Use of Cancer Survivors (FOCUS) Study, a population-based, cross-sectional study of ethnically diverse adult survivors of breast, prostate, colorectal, ovarian, and endometrial cancers from northern and southern California funded by the National Cancer Institute. Selected patients were mailed a detailed questionnaire to complete on their own and return in a postage paid envelope. Extensive telephone followup was conducted and additional questionnaire mailings were sent in efforts to reach patients and increase response rates. The study was approved by the institutional review boards at the Cancer Prevention Institute of California (CPIC, formerly known as the Northern California Cancer Center (NCCC)) and the University of Southern California (USC), Los Angeles, in accord with an assurance filed and approved by the US Department of Health and Human Services.

The cancer patients were selected from the CPIC and the Los Angeles County Cancer Surveillance Program, cancer registries that are members of the Surveillance, Epidemiology, and End Results (SEER) program. To be eligible, patients had to be English speaking, adults at least 21 years of age at diagnosis, have a primary diagnosis of breast, prostate, colorectal, ovarian, or endometrial cancer and have completed treatment. Case selection was stratified by cancer site, time since diagnosis, age group, and race/ethnicity to provide sufficient sample size in each subgroup for analyses. Specifically, time since diagnosis was dichotomized between an average of 6 (4 to 8) and 12 (10–15) years after initial cancer diagnosis. Age group included those <65 and 65+, while race/ethnicity was stratified by ethnicity/race: non-Hispanic White, African American, Hispanic White, and Asian American.

Of the 6,391 selected cases (not known to be deceased at the time of sample selection), 4,981 (78%) were eligible after we eliminated those who were found to be deceased after attempts to contact ($n = 415$), unable to understand English ($n = 477$), too ill to participate ($n = 289$), said they never had cancer ($n = 142$), whose physician did not provide consent ($n = 42$), or were otherwise ineligible ($n = 45$; e.g., in active treatment, out of the country). Of the 4,981 eligible, an additional 2,004 (40%) could not be located after multiple efforts were made to trace and locate them, (using web-based tracing services such as "reach411", "Intelius," "Masterfiles," and "Acxiom",) yielding a total of 2,977 eligible cases who were reached. Of these, 1,666 (56%) completed the mailed survey for the FOCUS study. Upon review of the surveys, a further 84 cases where the respondent indicated he/she was not in treatment were removed from all analyses leaving a final sample of 1,582 cases.

Multivariable logistic regression was used to determine factors related to participant response. Among the 4,981 eligible selected cases, those 65 and older, those with colorectal cancer, and those diagnosed longer ago were less likely to participate. Lastly, as this paper focused on outcomes for older adults (≥65 years of age), those in the sample younger than 65 ($N = 511$; 32%) were excluded resulting in an analytic sample that included 1,071 study respondents.

Eligible study participants were mailed a self-report study questionnaire containing a number of standardized measures to assess psychosocial and HRQOL variables along with questions assessing late health effects and follow-up care patterns specific to the larger FOCUS project. Included in the mailing was an introductory letter describing the purpose of the study and a prepaid return envelope. If the survey had not been returned after three weeks, the survivors were called to make sure they had received the questionnaire,

answer any questions, and encourage them to send in the questionnaire. Upon return of the completed questionnaire, study participants received either a $20 (LA County Cancer Surveillance Program) or $25 (CPIC) check and a thank you letter.

2.2. Measures

2.2.1. Demographic and Disease Characteristics. Self-reported socio-demographic information included age, sex, ethnicity/race, marital status, education, and health insurance. While household income was collected, the percent (11%) of missing data from this variable was significantly higher than the percent missing for education (1.4%); thus the decision was made to use education as a proxy for SES as opposed to both education and income. Additionally, income and education were highly correlated in this sample. Health-related characteristics, including type of treatment, cancer history, and disease stage were collected via SEER registry data. Based on SEER historic staging information, stage of disease was characterized as local, regional, and distant for breast, colorectal and gynecologic, whereas prostate cancer stage was differentiated as local and regional or distant. Times since diagnosis and comorbid medical conditions (checklist of 39 medical conditions, including irregular heartbeat, heart failure, cardiomyopathy, heart attack, angina, hypertension, pericarditis, leaking heart valves, blood clots, stroke, epilepsy, seizures, neuropathy, chronic lung disease, asthma, pleurisy, lung fibrosis, pneumonia, abnormal liver function, liver disease, inflammatory bowel disease, gallbladder problems, kidney stones, kidney or bladder infections, hyperthyroid, hypothyroid, diabetes, osteoporosis, avascular necrosis, partial or complete deafness, cataracts, problems with retina, arthritis, lymphedema, anemia, shingles, sciatica, and fertility issues) were collected via self-report. The comorbidity checklist was adapted from previous studies on cancer [14, 15].

2.2.2. Health-Related Quality of Life. Two summary scores from the Short Form–12 were used to measure HRQOL [16, 17]. These included the physical component summary (PCS) score and mental component summary (MCS) score constructed on the basis of the 1999 US population norms with a mean value of 50 that represented the US population norms and a standard deviation of 10.

2.2.3. Psychosocial Factors. The Life Orientation Test-Revised (LOT-R) was used to measure optimism [18]. The LOT-R is a 6-item scale including items such as "In uncertain times, I usually expect the best." The scale has exhibited good reliability and validity in use with chronically ill populations, including cancer patients [9, 19]. Cronbach's alpha for the six items in the current study was .93. The 12-item short form of the MOS Social Support scale was used to assess social support [20, 21]. For each item, the respondent was asked to indicate how often social support was available to him or her if needed. Response options ranged from "none of the time" to "all of the time." Items were summed and transformed into a scale of 0 to 100. Cronbach's alpha for the Social Support scale in the current study was .95. Perceived control was measured using a 4-item scale used in an earlier study. [14] Respondents were asked to indicate the extent of control they have over aspects of cancer, including "emotional responses to your cancer", "physical side effects of your cancer and its treatment", "the course of your cancer (i.e., whether cancer will come back or get worse)", and "the kind of follow-up care you receive for your cancer." Response options ranged from "no control at all" to "complete control". The four items were summed and transformed into a scale of 0 to 100. Cronbach's alpha for these four items was .88.

2.3. Analytic Plan. Descriptive statistics were used to describe the demographic, health, and psychosocial characteristics of the sample. Separate general linear models (GLMS) were run for all cancer sites combined as well as for each specific cancer site to test the main effects of independent variables (age, ethnicity/race, education, medical comorbidities, optimism, and social support) and the interaction effects of age and ethnicity/race on physical and mental health. Variables included in these multivariable models were significantly associated ($P < .05$) with HRQOL at the bivariate level using χ^2 tests for categorical variables and t tests for continuous variables. The following variables not associated with HRQOL in bivariate analyses were not included in the final model: gender, cancer stage, health insurance coverage, time since diagnosis, SEER site and type of cancer treatment received, and perceived control. Blocks of variables were entered into the models sequentially to examine the impact of each category of factors (demographic, health, and psychosocial) on HRQOL. Adjusted means and standard errors of outcome measures by categorical demographic and health characteristics were calculated using general linear modeling (GLM) and beta coefficients and standard errors of outcomes were generated for continuous variables. Tukey's post hoc tests were used to detect significant differences. Estimated marginal means were used to plot the effects of age and race on HRQOL. Analyses were conducted using SPSS version 16.

3. Results

3.1. Sample Characteristics. The analytic sample consisted of 1,071 men and women aged 65 years or older (Mean = 75.7, SD = 6.1) diagnosed with confirmed cases of breast, prostate, colorectal, or gynecologic cancer. The gynecologic cancer group included both endometrial and ovarian cancers due to insufficient sample sizes to permit separate analyses for each group. Table 1 displays other characteristics of the sample. Average time since diagnosis was 9 years (SD = 3.2). Two-thirds of the sample was represented by ethnic/racial minority groups providing sufficient sample size for testing age/race interaction effects on HRQOL. The sample consisted of slightly more ($P < .05$) females (61%) than males. Table 2 shows the mean scores and standard deviation for the psychosocial and HRQOL scales. Physical and mental HRQOL scores across all cancer sites were marginally lower

Table 1: Sample characteristics (%).

	Total $N = 1071$	Breast $N = 247$	Prostate $N = 314$	Colorectal $N = 274$	Gyn. $N = 236$
Current age					
65–74	43.4	36.4	40.5	43.4	41.5
75–84	26.0	27.5	25.5	22.6	29.2
85+	30.6	36.0	23.9	33.9	29.2
Race/ethnicity					
Non-Hispanic, White	33.6	31.5	25.7	33.1	42.3
Hispanic, White	19.6	19.8	24.4	17.3	16.9
African American	24.3	24.6	26.0	26.5	21.1
Asian American	22.4	24.1	23.9	23.2	19.7
Gender					
Male	38.4	—	100	50.6	—
Female	61.6	100	—	49.4	100
Education					
<High school	9.9	7.3	12.4	10.9	8.8
High school/GED	17.0	18.9	14.9	16.3	18.0
Some college/technical school	36.2	33.5	30.2	41.5	40.1
College graduate (or more)	36.9	39.6	42.5	31.3	33.1
Health insurance					
Yes	97.1	97.2	97.8	97.0	96.4
No	2.9	2.8	2.2	3.0	3.6
Stage (SEER)					
Localized	45.6	74.4	—	48.3	62.9
Regional	21.3	23.9	—	49.1	14.2
Distant	6.8	1.5	1.3	1.5	20.6*
Localized/regional (prostate only)	—	—	95.7	—	—
Unstaged	1.8	0.3	3.1	1.0	2.2
Comorbid medical conditions					
Mean (std)	5.4 ± 3.7	5.7 ± 4.0	4.8 ± 3.3	5.3 ± 3.6	5.6 ± 3.5
Current symptoms					
Mean (std)	6.3 ± 4.7	6.7 ± 4.4	5.2 ± 4.4	5.8 ± 4.7	7.2 ± 4.9

* The high rate of distant disease in the gynecologic group reflects higher rates of distant disease in African American women with endometrial cancer, which is comparable to rates in the US population.

Table 2: Unadjusted mean scores and standard deviations for psychosocial/HRQOL scales.

	Total	Breast	Prostate	Colorectal	Gynecologic
Optimism*	16.2 (3.8)	16.2 (3.7)	16.3 (3.7)	15.9 (3.8)	16.2 (3.8)
Social support†	80.4 (17.7)	79.1 (17.8)	82.6 (17.7)	80.5 (17.9)	78.8 (17.7)
Physical function‡	42.5 (11.4)	41.2 (11.4)	44.5 (11.2)	42.4 (11.6)	41.1 (11.4)
Mental function‡	52.1 (9.0)	51.4 (9.3)	52.8 (8.9)	51.9 (9.0)	52.1 (8.9)

* Scored on a 0–24 scale (higher scores reflect higher optimism).
† Scored on a 0–100 scale (higher scores reflect more social support).
‡ Constructed on the basis of the 1999 US population norms with a mean value of 50 that represented the US population norms and a standard deviation of 10. Higher scores reflect better function.

than general US population norms for individuals aged 65 years or older [16].

3.2. Correlates of HRQOL in Ethnically Diverse Older Adults with Cancer. Using the GLM procedure, adjusted mean scores were calculated to examine the association between demographic, health related, and psychosocial factors with physical and mental health (Table 3). The following section describes the results of the GLM procedure overall (all sites combined) and across the different cancer sites.

3.3. Physical HRQOL. The combined variables in the overall model accounted for 29% (adjusted R^2) of the variance in physical HRQOL with demographics accounting for 6%,

Table 3: Adjusted mean HRQOL scores[†] by demographic, health, and psychosocial characteristics.

	Overall		Breast		Prostate		Colorectal		Gynecologic	
	MCS	PCS	MCS	PCS	MCS	PCS	MCS	PCS	MCS	PCS
Demographic										
Age										
65–74	**50.9 (0.5)**[b]	**43.6 (0.5)**[b]	**49.3 (1.1)**[b]	**41.8 (1.2)**[b]	51.5 (0.8)	**46.8 (0.9)**[b]	51.6 (0.9)	**42.7 (1.1)**[b]	50.1 (1.0)	**42.1 (1.1)**[b]
75–84	**52.4 (0.5)**[a]	**41.9 (0.7)**[a]	**51.3 (1.2)**[a]	**40.4 (1.3)**[b,c]	52.2 (1.1)	**42.5 (1.2)**[a]	53.9 (1.1)	**41.4 (1.6)**[a]	52.1 (1.1)	**41.3 (1.3)**[b]
85+	**52.2 (0.5)**[a]	**39.6 (0.7)**[a]	**52.4 (1.1)**[a]	**36.6 (1.2)**[a]	52.1 (1.1)	**41.5 (1.3)**[a]	52.1 (1.1)	**39.2 (1.3)**[a]	51.6 (1.4)	**37.9 (1.5)**[a]
Race/ethnicity[‡]										
NHW	52.6 (0.5)	**42.6 (0.6)**[b]	**53.6 (1.1)**[b]	**40.4 (1.3)**[b]	**53.7 (1.1)**[b]	**40.4 (1.3)**[b]	**51.3 (1.1)**[a]	**42.9 (1.2)**[b]	52.8 (0.9)	42.2 (1.1)
HW	51.7 (0.7)	**43.4 (0.8)**[b]	**48.0 (1.4)**[a]	**41.9 (1.6)**[b]	**48.0 (1.4)**[a]	**41.9 (1.6)**[b]	**55.1 (1.5)**[b]	**40.6 (1.8)**[a]	51.7 (1.5)	42.1 (1.7)
AA	51.6 (0.6)	**40.2 (0.7)**[a]	**52.7 (1.3)**[b]	**38.1 (1.5)**[a]	**52.7 (1.3)**[b]	**38.1 (1.5)**[a]	**51.7 (1.4)**[a]	**39.9 (1.6)**[a]	48.3 (1.4)	38.5 (1.6)
Asian American	51.4 (0.7)	**40.6 (0.8)**[a]	**49.9 (1.4)**[a]	**37.9 (1.5)**[a]	**49.9 (1.4)**[a]	**37.9 (1.5)**[a]	**52.1 (1.4)**[a]	**41.1 (1.6)**[a]	52.2 (1.5)	38.8 (1.7)
Education										
<HS	**49.8 (0.8)**[b]	**40.4 (0.9)**[a]	49.8 (1.9)	**32.1 (2.1)**[a]	49.8 (1.9)	**32.1 (2.1)**[b]	49.4 (1.6)	**40.8 (1.9)**[b]	50.2 (1.8)	**40.7 (2.1)**[a]
HS/GED	**51.8 (0.7)**[a]	**40.2 (0.7)**[a]	51.6 (1.3)	**42.3 (1.5)**[b]	51.6 (1.3)	**42.3 (1.5)**[a]	54.2 (1.4)	**36.8 (1.7)**[a]	51.3 (1.3)	**37.7 (1.4)**[b,c]
Some C/T	**52.8 (0.5)**[a]	**41.8 (0.6)**[b]	52.3 (1.0)	**41.9 (1.2)**[b]	52.3 (1.0)	**41.9 (1.2)**[a]	52.6 (0.9)	**43.0 (1.2)**[b,c]	52.1 (1.1)	**40.6 (1.2)**[a]
College grad	**52.8 (0.5)**[a]	**44.4 (0.6)**[a]	50.6 (1.2)	**41.9 (1.3)**[b]	50.6 (1.2)	**41.9 (1.3)**[a]	53.9 (1.2)	**43.9 (1.4)**[b,c]	51.7 (1.2)	**42.6 (1.3)**[b]
Health										
Beta coef (SE)										
Comorbidity	**−0.5 (0.1)**	**−1.4 (0.1)**	**−0.5 (0.2)**	**−1.2 (0.2)**	**−0.5 (0.2)**	**−1.2 (0.2)**	**−0.4 (0.2)**	**−1.5 (0.2)**	**−0.4 (0.2)**	**−1.8 (0.2)**
Psychosocial										
Beta Coef. (SE)										
Social support	**0.1 (0.1)**	0.1 (0.1)	**0.2 (0.1)**	0.1 (0.1)	0.2 (0.1)	0.1 (0.1)	**0.2 (0.1)**	0.1 (0.1)	**0.2 (0.1)**	0.1 (0.3)
Optimism	**0.8 (0.1)**	**0.6 (0.1)**	**0.9 (0.1)**	0.2 (0.2)	**0.7 (0.2)**	**0.5 (0.2)**	**0.9 (0.1)**	**0.8 (0.2)**	**0.7 (0.2)**	**0.7 (0.2)**
Model Adj R^2	22.1	29.0	24.9	36.2	15.9	36.1	20.9	33.2	20.9	37.0

[†] Adjusted for all other variables in the model.

[‡] NHW: non-Hispanic White; HW: Hispanic White; AA: African American.

Note: values in bold indicate P value < .05 from overall F-test.

Different letters denote statistically significant differences using Tukey's post hoc tests.

comorbidity accounting for 19%, and psychosocial factors accounting for 5%. In the overall model, as well as the breast and prostate cancer group, the interaction effect between age and race was significant when entered into the models with the demographic factors, but the effect became nonsignificant in the overall model and breast cancer model once comorbidity was entered into the models. In the overall model, the pattern of interaction was such that African Americans in the 75–79 age group reported lower physical health than non-Hispanic Whites and Hispanic Whites in this age group (see Figure 1). This same pattern existed in the breast cancer group, but these data also showed that Hispanic Whites in the 75–79 age group reported higher physical health scores compared to African American and Asian Americans in this age group. The comorbid burden among all cancer sites combined, as well as the breast cancer group, is significantly ($P < .05$) greater than the comorbid burden in the prostate cancer group (Table 1). To explore this pattern further, analysis of variance was conducted to see if there was a differential comorbid pattern in African Americans in the 75–79 age group compared to other ethnic/racial groups in this age range. Results indicated that African American breast cancer survivors in this age group reported, on average, 9.6 comorbid conditions (SD = 5.5) compared with 5.3 for non-Hispanic Whites (SD = 3.7), 6.3 for Hispanic Whites (SD = 2.4), and 5.8 for Asian Americans (SD = 3.4) (all $P's < .05$). This pattern was similar in the overall model.

With respect to prostate cancer, the significant interaction persisted after entering comorbidity and other psychosocial variables into the model ($\beta = 9.16, SE = 4.5, P < .01$). African Americans and Asian Americans in the 75-79 age group reported lower PCS scores than non-Hispanic Whites and Hispanic Whites. These scores were greater in the oldest age group, (80 plus) for African Americans and Asian Americans with a significant difference between African Americans' scores and non-Hispanic Whites' scores on physical HRQOL (Figure 1).

Other findings of interest (see Table 3) include older age significantly associated with lower PCS scores, overall ($P < .01$) and in the breast and colorectal groups (all $Ps < .05$). PCS scores for African Americans and Asian Americans in the breast, prostate and "all sites combined" models were significantly lower than non-Hispanic Whites and Hispanic Whites ($P < .01$). Across all cancer sites, education was significantly associated (Cohen's d effect size = .3) with PCS in that those with a college degree and/or graduate degree had higher PCS scores than all those groups with lower educational attainment (all $Ps < .05$). A more pronounced relationship between low education and PCS was found in the breast and prostate groups where those survivors without a high school diploma or GED reported PCS scores nine points lower than the survivors with the same education in the colorectal and gynecologic groups. More comorbid conditions were significantly associated with worse PCS ($P < .01$), overall and across the four cancer sites. Social support was not related to PCS, but higher optimism was significantly associated with better PCS ($P < .01$) overall and across three of the four sites (i.e., breast cancer, nonsignificant).

3.4. Mental HRQOL. Investigation of MCS scores showed that the variance explained by the set of independent variables in the overall model was 22% (adjusted R^2). Unlike PCS scores, the psychosocial variables explained the majority of the variance in mental HRQOL with optimism = 11% and social support = 4%. The remaining variance was explained by demographics (4%) and health factors (3%). In contrast to PCS results, the age-race/ethnicity interaction effect was not significant in the overall model or site-specific models regardless of when it was entered into the model. Overall and in the breast cancer group older age was associated with higher MCS score (all $Ps < .05$). Additionally, having a college degree or having some college experience was significantly associated with higher scores on MCS compared with graduating from high school or obtaining a GED ($Ps < .01$) in the colorectal group and in all sites combined. Those with more comorbid conditions reported worse MCS ($P < .01$), overall and across the four cancer sites. The overall model as well as the site-specific models show higher scores on social support and optimism was significantly associated with higher scores on MCS ($Ps < .05$).

4. Discussion

This population-based study examined the HRQOL of older long-term cancer survivors by cancer type, ethnicity/race and age as well as potential interaction effects between age, ethnicity/race, and HRQOL. We found that the double jeopardy effect of being an ethnicity/racial minority and older persisted for the overall sample (all sites combined) and the breast cancer group when entered into the model with demographic variables, but the effect went away after controlling for comorbidity. Double jeopardy persisted in the prostate cancer group even after controlling for comorbidity. Different predictors accounted for differing amounts of variance in PCS and MCS scores. In general psychosocial factors were more strongly associated with MCS, while medical comorbidities were more strongly associated with PCS.

The presence of double jeopardy in the overall model (likely driven by the breast cancer group) as well as the breast cancer model could potentially be explained by the higher comorbid burden among African American cancer patients in the middle age group compared to this group in the other cancer sites. The importance of monitoring for comorbidities, especially in older minority breast cancer survivor populations, and ensuring adequate control of these conditions should be of particular concern and is becoming a growing focus of attention in the oncology community [22, 23].

There was evidence to support the existence of double jeopardy in our sample of prostate cancer survivors even after controlling for comorbid conditions. Future research should further explore this interaction as prostate cancer is the most prevalent cancer in older men and African American men are at greater risk compared to white men. Additionally, African American men generally have more advanced disease when diagnosed [24]—perhaps due to

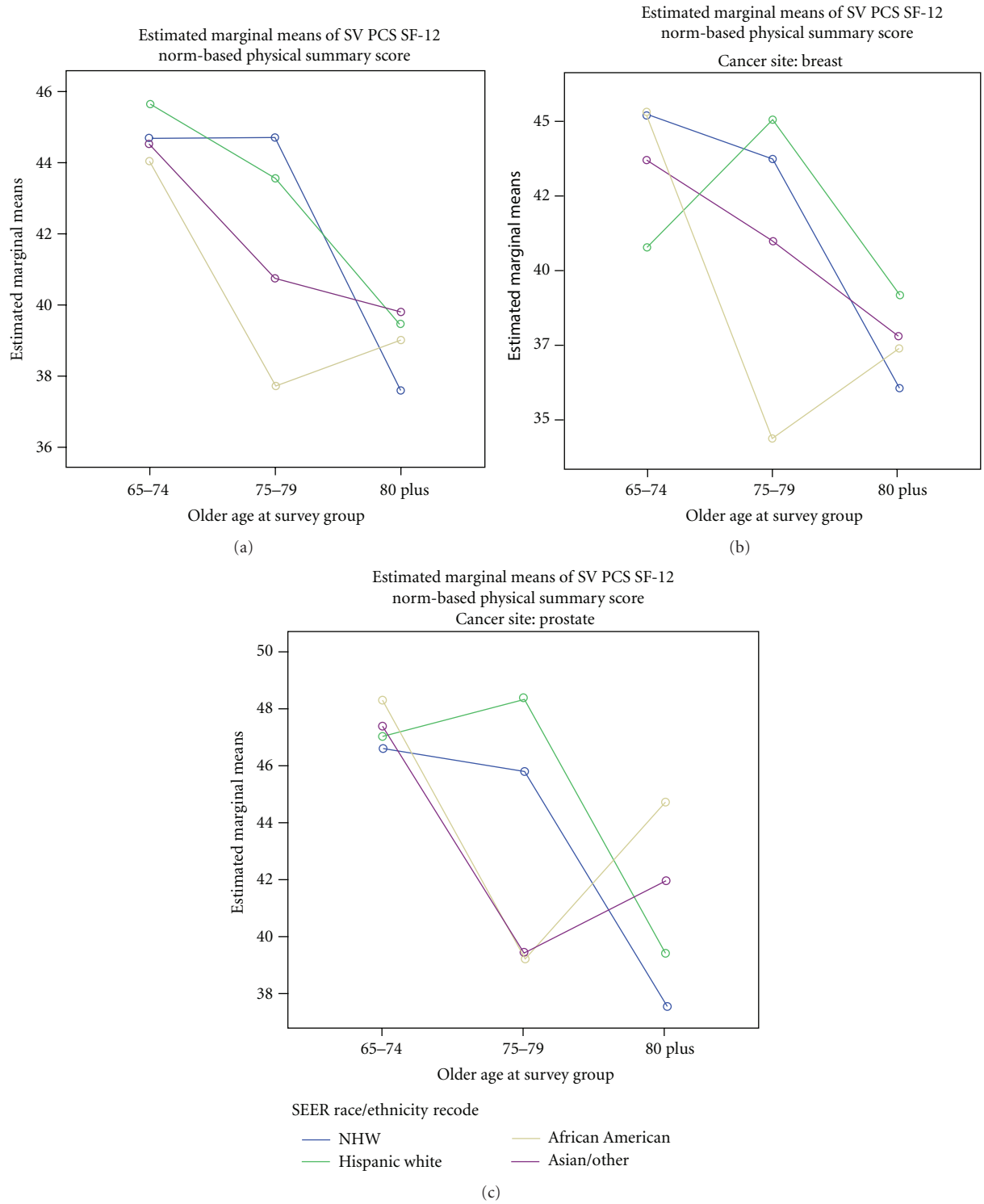

Figure 1: Age by race/ethnicity interaction plots (PCS).

delay in diagnosis because of poorer screening rates and access to care. However, stage of disease was not significantly related to HRQOL thus likely did not account for the presence of double jeopardy in this group. It is important to note that our prostate cancer group was quite homogeneous with respect to stage (95% local/regional), so there was little variability to adequately test the association of stage of disease on HRQOL in that group. Figure 1 suggests a higher score in physical function in the oldest age group for African American and Asian Americans compared to non-Hispanic

Whites perhaps suggesting a resiliency effect. It is conceivable that the oldest age group reflects a more adaptive and healthy cohort or the younger race-specific cohorts were exposed to events or treatments with long-term impacts on physical function. A healthy survivor bias may also explain this effect. Although there is a 6.2-year reduction in life expectancy at birth for African American males compared to White males, this narrows to 2.2 years at age 65 and only .7 years at age 75 (CDC, Health, United States, 2008). This suggests, that for those African American men who survive to age 75, black-white differences in health may not be as pronounced.

A few additional findings warrant special note. Consistent with other studies [8, 12], these data suggest that race/ethnicity influences physical functioning above and beyond socioeconomic status. African American and Asian American cancer survivors (all sites combined) reported significantly lower PCS scores compared with White and Hispanics, even after controlling for education. This effect also persisted after controlling for noncancer medical comorbidities. These data suggest that clinicians should potentially anticipate differences in older adults from some minority backgrounds, as they may be at risk for greater decrements in physical function as a result of their cancer and treatment. Level of education was found to positively influence not only survivors' reports of physical health (PCS) but also mental health (MCS). A buffering effect of education on illness outcomes has been shown by others [7, 8, 12] and may be a function of the association between more education and increased coping skills, better access to optimal healthcare, including preventive services (contributing to a stronger feeling of control over health care) and greater investment in positive health behaviors. To the extent that racial disparities continue to persist in access to education, this has implications for the future health of these populations.

Not surprisingly, the presence of competing comorbid conditions was found to adversely affect both mental and physical health outcomes. On average, the survivors in this study reported more than five non-cancer comorbidities. In some cases, with cancer survivors now living longer, comorbid condition may include the diagnosis of a second or third malignancy [25]. Careful assessment of comorbid conditions prior to cancer treatment and across the cancer survivorship trajectory is warranted in all populations of survivors.

Strengths of this study are its population-based stratified sampling method, inclusion of large numbers of older survivors, attention to long-term (5–14 years after diagnosis) survivors' function, and well-being, examination of the four cancer sites for which we have the most prevalent populations of survivors, as well as recruitment of sufficient numbers of minority groups to enable examination of race/ethnicity by age interaction effects on survivors' HRQOL outcomes. However, there are a number of limitations to these data. As noted earlier, those who were sicker, whether due to cancer or other comorbid conditions, non-English speaking, longer-term survivors, and those who were hard to reach (potentially because they had moved to locations where care is delivered by extended family or in assisted living or nursing home facility), did not participate in this survey. Thus, it is not clear how generalizable the present findings are to the broader population of older cancer survivors. This differential pattern of response (or dropout) could account for the unexpected observation that older (80 plus) prostate cancer survivors of Asian and African American background reported better physical HRQOL than their younger (75–79) counterparts. Although this is a cross-sectional study, it was nonetheless interesting to note that, while PCS scores for prostate cancer survivors were similar across ethnic/racial groups in the 65–74 age category, there was considerable divergence on this variable among those in the oldest age category. A further limitation to this study is that, while likely to be a rare occurrence, there is no way of knowing whether a caregiver or family member may have completed the surveys on the survivor's behalf.

Understanding the impact of cancer on HRQOL of older adults from minority backgrounds is of great importance. With the aging of Americans and demographic changes in the ethnic/racial composition of the US population, clinicians need to better anticipate, predict, and treat the physical and mental consequences of cancer and its treatment in specific segments of the population. The current study provides information regarding the physical and mental functioning of older adults from minority backgrounds as well as correlates that can be used to target clinical assessments and interventions. Our study suggests double jeopardy exists in the overall sample and breast cancer survivors, but is explained by differential burden of comorbid conditions in the middle age group for African Americans. Examining the reasons why double jeopardy persists in men with prostate cancer, after controlling for comorbidity warrants further attention. To what extent the compounding effect of age and race on physical function in the middle age group are the result of poorer access to care or delays in screening, and diagnosis in this group is not known, but worthy of future study.

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