Recent Trends in Cost-Related Medication Nonadherence Among Cancer Survivors in the United States

Min Jee Lee, MPH; M. Mahmud Khan, PhD; and Ramzi G. Salloum, PhD

ABSTRACT

BACKGROUND: Cancer survivors avoid necessary medications due to costs.

OBJECTIVE: To estimate the prevalence of cost-related medication non-adherence (CRN) by age and insurance status over a number of years in a national sample of U.S. cancer survivors.

METHODS: Using the 1999-2012 National Health Interview Survey, we examined the prevalence and correlates of self-reported CRN, that is, patient-reported inability to afford prescribed medications within the past 12 months, resulting in nonadherence among cancer survivors. Descriptive statistics and multivariate logistic regression models were used to identify time trends in CRN among cancer survivors.

RESULTS: In a nationally representative sample of 20,517 cancer survivors from 1999 to 2012, 1,788 (8.7%) survivors reported CRN, representing approximately 436,498 individuals nationally. CRN increased significantly from 11.8% (1999-2005) to 16.9% (2006-2012) among younger cancer survivors ($P < 0.001$). Among young cancer survivors (aged 45-64 years), the uninsurance rate was higher for those reporting CRN in the years 2006-2012 (48.5%) than in the earlier period (42.5%; $P = 0.043$). Among older cancer survivors, insurance coverage through Medicare only was lower for individuals reporting CRN in the years 2006-2012 (5.8%) than in the earlier period (7.8%; $P = 0.0210$). In adjusted models, younger cancer survivors without health insurance were more likely to report CRN than those with supplemental private insurance with Medicare, and older cancer survivors with Medicare only were more likely to report CRN than those with supplemental private insurance with Medicare.

CONCLUSIONS: Increasing trends in CRN were evident among younger cancer survivors.

J Manag Care Spec Pharm. 2018;24(1):56-64

Copyright© 2018, Academy of Managed Care Pharmacy. All rights reserved.

What this study adds

- This study examined trends in CRN over the years by age and insurance status in a national sample of U.S. cancer survivors.
- A significant increasing trend in the prevalence of CRN among younger cancer survivors was found, even after adjusting for race, gender, region, household income, educational attainment, number of comorbidities, self-rated health, activity limitation, and cancer site.

The cost of prescription drugs has continued to increase rapidly over the past few decades. By 2012, the aggregate expenditures on prescription drugs reached \$263 billion, or 9.7%, of total U.S. health expenditures.¹ Increases in drug costs have placed an increased financial burden on patients. This increased burden has led cancer survivors to lower dosage and frequency of drugs below the recommended level and to avoid filling prescriptions to reduce medical costs.^{2,3} Cost-related medication nonadherence (CRN) is associated with a wide range of negative health outcomes in many chronically ill adults, including poorer physical and mental functioning, myocardial infarction, stroke, increased use of emergency and hospital services, and death.^{4,5}

Increases in medical care cost is associated with the substantial increase in out-of-pocket expenses of cancer patients and their family members during diagnosis, treatment, and follow-up care.^{6,7} Increased treatment cost has been shown to be a factor in medication nonadherence.⁶ One study found that Medicare breast cancer survivors treated with aromatase inhibitors experienced higher levels of financial difficulties than breast cancer survivors treated with less expensive tamoxifen.⁸ Financial stress is a significant concern for cancer survivors with a history of chemotherapy and radiation, and financial difficulties often lead to skipping prescribed medications.⁹

Previous studies have examined CRN and its risk factors among cancer survivors.¹⁰⁻¹³ Lee et al. (2016) investigated gender-specific differences in the prevalence of CRN using the National Health Interview Survey (NHIS) and found that female cancer survivors were more likely to report CRN and that having any type of insurance reduced CRN.¹⁰ Another study estimated the prevalence of CRN by race and ethnicity and found that older African-American and Hispanic cancer survivors were more likely to report CRN compared with

What is already known about this subject

- The cost of prescription drugs has continued to increase rapidly over the past few decades.
- The increased cost burden of prescription drugs has led cancer survivors to lower dosages and frequency of drugs below recommended levels and to avoid filling prescriptions to reduce medical costs.
- Cost-related medication nonadherence (CRN) is associated with a wide range of negative health outcomes, and previous studies have identified a number of factors associated with CRN.

non-Hispanic whites.¹¹ Moreover, Nekhlyudov et al. (2011) investigated CRN among elderly Medicare enrollees using the 2005 Medicare Current Beneficiary Survey and found that lower income, having nonemployer-based medication insurance, and being African American were significant risk factors.¹² Nekhlyudov et al. also found that approximately 10% of elderly Medicare beneficiaries with and without cancer reported CRN and lowered expenditures on basic needs to offset the high cost of medications.¹² Sabatino et al. (2006) examined CRN among U.S. adult cancer survivors aged 18-64 years, using the 1998 and 2000 NHIS and found that uninsured and publicly insured survivors were more likely to experience CRN.¹³ They also found that greater than 20% of cancer survivors reported delaying or missing needed care within the previous year because of cost and that those unmet needs were greatest among cancer survivors with health insurance coverage; 42.8% of this group reported that they did not obtain needed prescription drugs because of cost.¹³

Although a number of studies have examined the factors associated with CRN, little is known about the CRN trend over the years because of the economic downturn and health policy changes. To understand the trend in CRN, we have estimated the incidence of CRN using a national sample of cancer survivors for the years 1999-2012. Our dataset covers 7 years (1999-2005) before the introduction of Medicare Part D and 7 years after (2006-2012).

We had 2 main research questions. First, we hypothesized that, because of the rapid increase in prices of prescription drugs, CRN should show an increasing trend among younger cancer survivors (aged 45-64 years) and, in particular, those without any health insurance coverage. Given that many survivors in this age group lack health insurance coverage,^{13,14} and higher out-of-pocket costs were strongly associated with non-adherence to therapy,¹⁵ we suspected that CRN would increase among younger cancer patients. Thorpe et al. (2003) found that 11% of cancer survivors aged <65 years lacked insurance primarily near the time of diagnosis.¹⁴

Second, we hypothesized that CRN should show a declining trend among older cancer survivors, particularly among those with Medicare.

Methods

Data Source

We used data from the NHIS, a cross-sectional household-based, nationally representative survey that has been conducted annually by the National Center for Health Statistics since 1957.^{16,17} We combined data from annual waves of the survey from 1999 through 2012 to obtain a sample of cancer survivors in order to observe long-term trends in CRN. The NHIS uses a complex survey design that includes clustering, stratification, and multistage sampling to collect self-reported health data from a representative sample of the civilian, noninstitutionalized U.S. population.¹⁸

Study Sample

Cancer survivors were identified as those who answered “yes” to the question “Have you ever been told by a doctor that you had cancer?”. Respondents who were younger than 45 years were excluded from the analysis because cancer survivors in the age group 20-39 years are often diagnosed with different types of cancers than those traditionally seen in adult oncology clinics.¹⁹ For our analyses, we excluded respondents with a diagnosis of non-melanoma skin cancers because of their distinctly different treatment strategies and prognoses.¹⁰ The resulting dataset included information on 22,488 cancer survivors aged 45 years or older. In the dataset, 427 participants did not report their race; 176 did not report their educational status; 1,029 did not report their household income levels; 251 did not report their health insurance status; 50 did not report their self-rated health status; and 154 participants did not report their cancer type. After excluding all cases with at least 1 missing piece of relevant data (n=1,971), a total of 20,517 cancer survivors were included in the analysis.

Statistical Analysis

The main dependent variable of interest was CRN, which was defined as the self-reported inability to afford prescribed medications with the result of not taking medication within the previous 12 months. Inability to afford medications was identified by respondents who answered “yes” to the following question: “During the past 12 months, was there a time when you did not take your prescribed medication because of cost? Do not include over-the-counter medication.”

The dependent variable was a binary variable (yes/no). The main independent variable of interest was time in years. We examined CRN by age (in years) and insurance status across time in a national sample of U.S. cancer survivors, and time or year was included in the analysis as a continuous variable ranging from 1 to 14. We stratified the analyses into groups composed of individuals aged 45-64 years (younger patients) and individuals aged 65 years or older (older patients) because U.S. adults generally qualify for Medicare at age 65, and previous research has found that age modifies access to medications among cancer survivors.^{20,21}

A number of research studies have found that insurance type or enrollment in insurance plans modifies access to medications among cancer survivors.^{13,20,22} Therefore, health insurance type was categorized into 1 of 7 groups: Medicare with supplementary private insurance, private health insurance only, Medicaid only, Medicare only, Medicare and Medicaid dual coverage, other insurance, and uninsured. To simplify health insurance type, we combined remaining health insurance types into an “other” category that included TRICARE, VA, SCHIP, and other military coverage. Gender was categorized as male or female. Race was self-reported and categorized as non-Hispanic white, black or African American, and other.

Recent Trends in Cost-Related Medication Nonadherence Among Cancer Survivors in the United States

TABLE 1 Characteristics of Cancer Survivors by Age Group and Time: National Health Interview Survey, 1999-2012

Characteristic	Aged 45-64 Years						Aged ≥ 65 Years					
	1999-2005			2006-2012			1999-2005			2006-2012		
	n	Weighted (n, %)		n	Weighted (n, %)		n	Weighted (n, %)		n	Weighted (n, %)	
Total	4,015	912,432	100.0	4,139	1,132,385	100.0	6,325	1,467,102	100.0	6,038	1,682,230	100.0
CRN												
Yes	498	107,355	11.8	713	191,459	16.9	312	69,232	4.7	265	68,452	4.1
No	3,517	805,077	88.2	3,426	940,925	83.1	6,013	1,397,870	95.3	5,773	1,613,778	95.9
Insurance type												
Supplemental private with Medicare	114	27,348	3.0	135	37,918	3.3	3,928	942,965	64.3	3,307	963,132	57.3
Private insurance only	2,739	636,671	69.8	2,530	723,752	63.9	250	58,226	4.0	125	34,995	2.1
Medicare only	171	37,359	4.1	278	68,581	6.1	1,682	370,882	25.3	2,151	575,177	34.2
Medicare and Medicaid	280	58,639	6.4	335	80,104	7.1	465	95,028	6.5	455	108,926	6.5
Medicaid only	132	28,521	3.1	196	49,956	4.4						
Other	175	37,125	4.1	234	59,987	5.3						
Uninsured	404	86,769	9.5	431	112,086	9.9						
Medicare Part D	—	—	—	324	83,617	7.4	—	—	—	2,312	1,682,230	37.2
Sex												
Male	1,350	312,482	34.2	1,422	389,304	34.4	2,675	622,354	42.4	2,660	723,597	43.0
Female	2,665	599,950	65.8	2,717	743,080	65.6	3,650	844,747	57.6	3,378	958,633	57.0
Race												
White	3,498	822,056	90.1	3,205	966,445	85.3	5,787	1,370,417	93.4	4,996	1,494,744	88.9
Black	390	66,157	7.3	556	104,173	9.2	442	77,084	5.3	677	118,853	7.1
Other	127	24,218	2.7	378	61,766	5.5	96	19,601	1.3	365	68,633	4.1
Region												
Northeast	694	168,126	18.4	722	215,654	19.0	1,180	287,154	19.6	1,061	317,629	18.9
Midwest	952	223,833	24.5	996	285,059	25.2	1,611	386,200	26.3	1,495	429,895	25.6
South	1,510	345,262	37.8	1,525	408,515	36.1	2,280	524,750	35.8	2,240	606,172	36.0
West	859	175,212	19.2	896	223,156	19.7	1,254	268,997	18.3	1,242	328,534	19.5
Household income												
<\$35,000	1,756	384,705	42.2	1,658	424,898	37.5	4,493	1,034,558	70.5	3,345	913,129	54.3
\$35,000 to <\$75,000	1,282	293,968	32.2	1,232	348,070	30.7	1,367	323,088	22.0	1,858	531,027	31.6
≥\$75,000	977	233,759	25.6	1,249	359,417	31.7	465	109,456	7.5	835	238,074	14.2
Education												
No high school graduate	639	130,755	14.3	541	128,127	11.3	1,833	407,581	27.8	1,353	353,922	21.0
High school graduate	1,191	270,639	29.7	1,146	312,982	27.6	2,010	473,698	32.3	1,907	533,573	31.7
Some college and more	2,185	511,039	56.0	2,452	691,276	61.0	2,482	585,823	39.9	2,778	794,735	47.2
Number of comorbidities												
0-1	1,399	319,762	35.0	1,083	309,108	27.3	1,221	280,449	19.1	774	211,672	12.6
2-3	2,177	494,562	54.2	2,350	638,174	56.4	3,915	910,253	62.0	3,729	1,043,362	62.0
4+	439	98,109	10.8	706	185,103	16.3	1,189	276,400	18.8	1,535	427,196	25.4
Self-rated health												
Excellent, very good, good	2,740	637,353	69.9	2,790	787,017	69.5	4,157	980,399	66.8	4,186	1,191,038	70.8
Fair or poor	1,275	275,079	30.1	1,349	345,368	30.5	2,168	486,703	33.2	1,852	491,192	29.2
Activity limitation												
No	1,772	409,778	44.9	1,645	460,335	40.7	1,897	439,212	29.9	1,709	474,983	28.2
Yes	2,243	502,654	55.1	2,494	672,050	59.3	4,428	1,027,890	70.1	4,329	1,207,247	71.8
Cancer site or type												
Prostate	247	53,964	5.9	309	82,779	7.3	973	222,393	15.2	1,063	286,266	17.0
Melanoma	300	71,902	7.9	340	99,386	8.8	288	69,845	4.8	367	105,405	6.3
Hematologic	171	38,290	4.2	204	55,806	4.9	214	52,072	3.5	245	69,418	4.1
Colorectal	222	50,059	5.5	229	61,923	5.5	707	162,748	11.1	545	152,194	9.0
Breast	833	186,507	20.4	887	235,138	20.8	1,343	312,379	21.3	1,312	367,332	21.8
Cervix	359	82,988	9.1	401	111,382	9.8	167	38,417	2.6	167	45,194	2.7
Other	1,883	428,721	47.0	1,769	485,970	42.9	2,633	609,249	41.5	2,339	656,421	39.0

Note: Comorbidities were categorized to include coronary heart disease, hypertension, emphysema, stroke, asthma, heart condition/disease, and arthritis.
CRN=cost-related medication nonadherence.

FIGURE 1 Percentage of U.S. Cancer Survivors with CRN by Age Group and Year

CRN = cost-related medication nonadherence.

U.S. region of residence at the time of the interview was categorized as Northeast, Midwest, South, and West. Respondents self-reported the highest grade of school completed, which was categorized as no high school diploma, high school diploma, and greater than a high school diploma. Three categories of household income were defined: lower than \$35,000, \$35,000-\$75,000, and higher than \$75,000. From the dataset, it was not possible to identify Medicare beneficiaries with Medicare Part D insurance for the same time frame related to CRN.

The number of comorbidities was categorized into 3 groups (0-1, 2-3, and 4 or more). To measure comorbidities, we accounted for the number of self-reported medical conditions, including coronary heart disease, hypertension, emphysema, stroke, asthma, heart condition, and arthritis. Self-rated health was categorized as good or better (excellent, very good, and good) and fair or poor. Activity of daily living limitations (ADLL) was categorized as "yes/no," with "yes" indicating the presence of at least 1 ADLL.

We stratified the analyses into groups composed of individuals aged 45-64 years and those aged 65 years or older. Within each age stratum, we stratified the time period 1999-2005 and 2006-2012. For empirical analysis of CRN, descriptive and inferential approaches were used. Descriptive statistics summarized participant characteristics and the distribution of CRN by patient characteristics and by potential factors affecting CRN.

Chi-square statistics were used for testing differences in the values of different variables, including insurance type, gender, race, region, household income, education, number of comorbidities, self-rated health, activity of daily living limitations, and cancer site between years 1999-2005 and years 2006-2012. In addition, the weighted percentage of individuals reporting CRN was calculated for insurance type, gender, race, region, household income, education, number of comorbidities, self-rated health, activity of daily living limitations, and cancer site.

Multivariate logistic regression models, stratified by the 2 age groups, were used to calculate the adjusted associations between insurance type, time, and the outcome measure. Time was examined as a count variable in Table 4 and as a group variable (1999-2005 vs. 2006-2012) in Tables 1, 2, and 3. The odds ratios (ORs) with 95% confidence intervals (CI) were calculated to measure the strength of association between factors affecting CRN and incidence of CRN.

Sampling weights were derived by comparing the number of individuals in the dataset with national estimates of cancer survivors for each of the years. This comparison ensured that the survey weights could be used to obtain national values and proportions when a subset of NHIS data was included in the analysis. After applying the weights to the sample, the unweighted count of 20,517 cancer survivors represented 5.2 million cancer survivors, the aggregate number of U.S. cancer survivors aged 45 years or older for the years 1999-2012.

TABLE 2 Cancer Survivors Who Were Not Able to Afford Prescription Medications by Age Group and Time: National Health Interview Survey, 1999-2012

Characteristic	Aged 45-64 Years					Aged ≥ 65 Years				
	1999-2005		2006-2012		P Value	1999-2005		2006-2012		P Value
	n	%	n	%		n	%	n	%	
Total	498	5.3	713	9.4		312	2.2	265	2.2	
Insurance type										
Supplemental private with Medicare	16	14.1	30	20.4	0.077	137	3.3	97	2.7	0.171
Private insurance only	138	4.7	218	8.8		7	2.4	6	4.7	
Medicare only	54	31.5	93	34.8		131	7.8	127	5.8	
Medicare and Medicaid	35	23.9	45	23.5		37	7.9	35	6.7	
Medicaid only	65	24.4	81	23.7						
Other	19	10.5	39	17.2						
Uninsured	171	42.5	207	48.9						
Sex										
Male	123	8.9	201	13.5	0.528	91	3.2	106	3.7	0.001
Female	375	13.3	512	18.7		221	5.8	159	4.3	
Race										
White	415	11.3	498	15.8	0.001	267	4.5	173	3.5	<0.0001
Black	65	16.7	122	21.4		38	8.1	63	9.3	
Other	18	14.4	93	27.2		7	7.1	29	7.4	
Region										
Northeast	62	8.9	97	13.5	0.080	43	3.5	37	3.1	0.013
Midwest	97	9.9	157	15.9		67	3.9	59	3.7	
South	212	13.1	318	20.4		144	6.2	107	4.4	
West	127	14.3	141	15.0		58	4.4	62	4.9	
Household income										
<\$35,000	391	21.7	514	31.2	0.009	285	6.1	208	6.1	<0.0001
\$35,000 to <\$75,000	86	6.4	149	13.0		21	1.6	46	2.1	
≥ \$75,000	21	2.2	50	3.8		6	1.1	11	0.9	
Education										
No high school graduate	144	20.8	147	26.0	0.005	130	6.9	94	6.4	0.012
High school graduate	137	11.7	214	19.1		95	4.7	74	3.9	
Some college and more	217	9.5	352	14.2		87	3.3	97	3.2	
Number of comorbidities										
0-1	101	6.9	89	7.9	0.001	32	2.4	17	1.7	0.000
2-3	272	11.6	397	17.0		172	4.2	129	3.1	
4+	125	28.4	227	31.7		108	8.7	119	7.7	
Self-rated health										
Excellent, very good, good	209	7.1	304	11.2	0.213	129	2.9	115	2.5	0.685
Fair or poor	289	22.5	409	30.0		183	8.3	150	7.9	
Activity limitation										
No	94	4.9	122	7.3	0.600	38	1.8	27	1.4	0.495
Yes	404	17.4	591	23.5		274	6.0	238	5.1	
Cancer site or type										
Prostate	21	8.2	39	10.9	0.105	29	2.5	42	3.0	0.012
Melanoma	21	6.5	45	13.6		12	4.2	16	5.4	
Hematologic	28	12.9	35	17.2		12	5.0	11	3.7	
Colorectal	24	10.6	27	10.4		31	4.4	16	2.8	
Breast	72	8.4	105	11.3		62	4.3	50	3.3	
Cervix	69	18.6	116	31.3		16	10.1	14	7.4	
Other	263	13.3	346	18.8		150	5.5	116	4.8	

Note: Comorbidities were categorized to include coronary heart disease, hypertension, emphysema, stroke, asthma, heart condition/disease, and arthritis.

TABLE 3 Association of Insurance Type with CRN Among Cancer Survivors: National Health Interview Survey, 1999-2012

Insurance type	Aged 45-64 Years (n=8,154)				Aged ≥ 65 Years (n=12,363)			
	1999-2005		2006-2012		1999-2005		2006-2012	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Supplemental private with Medicare	1.00			1.00			1.00	1.00
Private insurance only	0.63	0.38-1.06	1.03	0.58-1.82	0.94	0.41-2.16	2.31	0.92-5.80
Medicare only	2.07	1.09-3.94	1.54	0.89-2.68	2.18	1.65-2.87	1.68	1.18-2.38
Medicare and Medicaid	1.16	0.58-2.31	0.72	0.35-1.49	1.07	0.67-1.72	0.95	0.58-1.56
Medicaid only	1.21	0.66-2.22	0.82	0.46-1.47				
Other	0.83	0.42-1.64	1.02	0.50-2.06				
Uninsured	5.64	3.13-10.17	5.30	3.0-9.20				

Notes: Reference group is supplemental private with Medicare. Adjusted for race, sex, region, household income, education, comorbidities, self-rated health, activity limitation, and cancer site. Bold numbers indicate statistical significance.

CI=confidence interval; CRN=cost-related medication nonadherence; OR=odds ratio.

All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

The characteristics of adults with a history of cancer, stratified by age group and survey year, are summarized in Table 1. The final sample had 20,517 cancer survivors aged 45 years or older, which represented an estimated 5.2 million U.S. cancer survivors. Younger cancer survivors were slightly more likely than older cancer survivors to be female and black or African American. Younger cancer survivors reported higher CRN, higher household income, higher educational attainment, and less activity limitations than older cancer survivors. From 1999 to 2005, 96% of older cancer survivors had Medicare alone or Medicare with private insurance or Medicaid. Medicare coverage of elderly cancer survivors increased to about 98% during 2006-2012. For younger cancer survivors, private insurance coverage was 70% during 1999-2005 and 64% during 2006-2012. Lower private insurance coverage during 2006-2012 compared with 1999-2005 was offset by increased coverage through public insurance programs, keeping the uninsurance rate more or less similar over these 2 time frames for the younger group. Therefore, these 2 age groups differed significantly in terms of insurance status and type of insurance coverage.

Figure 1 presents the percentage of U.S. cancer survivors who did not take needed prescription drugs because of cost. During the period from 1999 to 2012, 1,788 cancer survivors reported CRN (8.7%). Among younger cancer survivors, the prevalence of CRN increased from 9.9% in 1999 to 16.9% in 2012 ($P<0.0001$). The prevalence of CRN increased from 2.4% to 3.5% in 2012 for older cancer survivors as well ($P=0.039$).

Table 2 shows the characteristics of cancer survivors reporting CRN. Among younger cancer survivors (aged 45-64 years), the rate of uninsured status was higher in cancer survivors reporting CRN in the years 2006-2012 (48.5%) compared with

the earlier period (42.5%; $P=0.0434$). Among older cancer survivors, insurance coverage through Medicare only was lower among cancer survivors reporting CRN in the years 2006-2012 (5.8%) compared with the earlier period (7.8%; $P=0.0210$).

Table 3 describes the association between insurance type and CRN among cancer survivors. Younger cancer survivors with Medicare only were more likely to report CRN compared with those with Medicare and supplemental private insurance in 1999-2005 after adjusting for race, gender, region, household income, educational attainment, number of comorbidities, self-rated health, activity limitation, and cancer site (OR=2.07, 95% CI=1.09-3.94); however, this association was not significant in 2006-2012. Having any type of insurance was an important protective factor for CRN among younger cancer survivors. More specifically, younger cancer survivors without health insurance were more likely to report CRN than those with supplemental private insurance with Medicare in 1999-2005 (OR=5.64, 95% CI=3.13-10.17) and in 2006-2012 (OR=5.30, 95% CI=3.05-9.20). Older cancer survivors with Medicare only were more likely to report CRN than those with supplemental private insurance with Medicare, although the OR declined in the years 2006-2012 (1999-2005: OR=2.18, 95% CI=1.65-2.87; 2006-2012: OR=1.68, 95% CI=1.18-2.38). CRN remained higher for the older group, with Medicare coverage only compared with the group with Medicare along with private supplemental insurance.

Table 4 shows the multivariate logit model of variables associated with CRN among cancer survivors. In addition to the variables listed in Table 3, we included year of survey as a count variable to estimate the time trend. Introduction of this variable marginally decreased ORs relative to the model in Table 3. Among younger cancer survivors, there was an increasing trend in CRN from 1999-2012, and this trend persisted among younger cancer survivors even after adjusting for all relevant covariates. Moreover, those without health

TABLE 4 Multivariate Logit Model of Variables Associated with CRN Among Cancer Survivors: National Health Interview Survey, 1999-2012

Variables	Aged 45-64 Years (n=8,154)		Aged ≥ 65 Years (n=12,363)	
	OR	95% CI	OR	95% CI
Survey year	1.06	1.04-1.08	0.99	0.96-1.01
Health insurance coverage				
Supplemental private with Medicare	1.00		1.00	
Private insurance only	0.85	0.57-1.28	1.40	0.75-2.60
Medicare only	1.67	1.12-2.50	1.89	1.53-2.35
Medicare and Medicaid	0.84	0.51-1.39	1.03	0.74-1.43
Medicaid only	0.96	0.63-1.49		
Other	0.97	0.58-1.61		
Uninsured	5.40	3.57-8.17		
Sex				
Male	1.00		1.00	
Female	1.58	1.29-1.95	1.25	0.97-1.63
Race				
White	1.00		1.00	
Black	0.96	0.75-1.23	1.85	1.42-2.43
Other	1.32	0.96-1.82	1.50	0.98-2.29
Region				
Northeast	1.00		1.00	
Midwest	0.93	0.70-1.24	1.09	0.78-1.51
South	1.12	0.86-1.45	1.33	0.99-1.78
West	1.10	0.80-1.51	1.43	1.02-2.01
Household income				
< \$35,000	1.00		1.00	
\$35,000 to < \$75,000	0.48	0.39-0.59	0.39	0.29-0.53
≥ \$75,000	0.20	0.14-0.27	0.23	0.13-0.41
Education				
No high school graduate	1.00		1.00	
High school graduate	1.06	0.85-1.32	0.93	0.73-1.20
Some college and more	1.26	1.03-1.54	0.89	0.69-1.14
Number of comorbidities				
0-1	1.00		1.00	
2-3	1.58	1.28-1.96	1.42	1.03-1.97
4+	2.46	1.87-3.24	2.58	1.84-3.62
Self-rated health				
Excellent, very good, good	1.00		1.00	
Fair or poor	1.59	1.31-1.93	1.91	1.58-2.32
Activity limitation				
No	1.00			1.00
Yes	2.05	1.65-2.54	1.95	1.48-2.58
Cancer site or type				
Prostate	1.00		1.00	
Melanoma	1.04	0.63-1.71	1.85	1.11-3.08
Hematologic	1.20	0.72-1.99	1.23	0.69-2.18
Colorectal	0.65	0.39-1.09	1.00	0.64-1.56
Breast	0.66	0.41-1.04	1.07	0.70-1.64
Cervix	1.49	0.91-2.43	1.97	1.15-3.38
Other	1.02	0.68-1.52	1.43	1.02-2.01

Note: Bold numbers indicate statistical significance.

CI=confidence interval; CRN=cost-related medication nonadherence; OR=odds ratio.

insurance coverage were 5.40 times more likely to report CRN than those with supplemental private insurance with Medicare (95% CI=3.57-8.17). Note that insurance coverage is also time dependent, but the coefficient of the year variable should be able to indicate potential effects of increasing cost and price of medicines after controlling for insurance status and other individual level factors.

Discussion

In this nationally representative sample of U.S. cancer survivors, 8.7% (an estimated 436,498 individuals nationally) reported CRN from 1999 to 2012. A significantly increasing trend in the prevalence of CRN was evident among younger cancer survivors over the years ($P<0.001$). The prevalence of CRN showed no time trend for the years 1999-2012 for the older cancer survivors. Among younger cancer survivors (aged 45-64 years), uninsured status was found to be a significant risk factor of CRN. For younger and older patients, risk of CRN was found to be higher for individuals with Medicare only coverage. Therefore, having Medicare coverage alone does not protect individuals effectively against CRN. Among younger patients, prevalence of CRN was higher among female patients, although it did not show any statistical differences by race after controlling for insurance status, income, region, household income, educational attainment, number of comorbidities, self-rated health, activity limitation, and cancer site. For older patients, race was an important factor affecting prevalence of CRN; African Americans were 85% more likely to experience CRN compared with whites, after controlling for other potential covariates.

Household income was clearly an important factor affecting prevalence of CRN for both younger and older patients. The likelihood of reporting CRN declined rapidly with the increase in household income. Increasing number of comorbidities also tended to increase the prevalence of CRN for all patients, and the likelihood ratios of the variable were similar for younger and older patients. Activity limitations and fair or poor health status increased the prevalence of CRN.

Although this study was not designed to examine the effects of Medicare Part D on the prevalence of CRN, it is interesting to note that the rate of CRN for the period 2006-2012 was not lower than the rate in 1999-2005 for cancer survivors. Medicare Part D was introduced in 2006, and the expectation was that the prevalence of CRN would decline significantly after 2006, especially for older patients. About 98% of older patients were covered by Medicare alone or Medicare with other types of insurance. For this patient group, the decline in the prevalence of CRN in 2006-2012 from the 1999-2005 level was not statistically significant.

For younger patients, the CRN was significantly higher in the period 2006-2012 compared with the 1999-2005 level. This increase in CRN can be explained by the time trend in CRN and the changes in insurance status of the population over the years. Less than 15% of younger patients were covered by Medicare even in the 2006-2012 period. According to Yin et al. (2008), Medicare Part D coverage resulted in modest increases in average drug use among Medicare Part D beneficiaries.²² Langa et al. (2004) showed that a previous history of cancer was associated with an additional \$240 per year in out-of-pocket expenditures, whereas current cancer treatment was associated with an additional \$670 per year in out-of-pocket expenditures, even after adjusting for differences in sociodemographics, living situation, functional limitations, comorbid chronic conditions, and insurance coverage.⁶ Increasing out-of-pocket expenses is likely one of the factors contributing to the CRN time trend.

Limitations

This study has some limitations to consider. First, patients were asked to report CRN over the previous 12 months, so the possibility of recall bias is always present. Second, although the NHIS was conducted by trained interviewers, the survey did not verify reported medical conditions and care utilization with medical records. Finally, the survey suffers from selection bias, since less healthy patients, who are likely to be institutionalized, are not in the sample. The effect of Medicare Part D coverage could not be evaluated in this study because of the difficulty in defining the Part D coverage for the time frame over which CRN was defined. Moreover, only 37% of the older patients of the study (older than 65 years), were enrolled in Part D.

Conclusions

In this nationally representative study, we found that younger cancer survivors without health insurance were more likely to report CRN than those with supplemental private insurance with Medicare, and older cancer survivors with Medicare only were more likely to report CRN than those patients with supplemental private insurance with Medicare, even after controlling for variables such as race, gender, region, household income, educational attainment, number of comorbidities, self-rated health, activity limitation, and cancer site. This finding is especially true for uninsured younger cancer survivors who faced the largest cost barriers to prescribed medication. Approximately 14.6% of younger cancer survivors reported inability to afford medications in recent years.

Authors

MIN JEE LEE, MPH, and M. MAHMUD KHAN, PhD, Arnold School of Public Health, University of South Carolina, Columbia.
RAMZI G. SALLOUM, PhD, University of Florida College of Medicine, Gainesville.

AUTHOR CORRESPONDENCE: M. Mahmud Khan, PhD, Department of Health Services Policy and Management, Arnold School of Public Health, University of South Carolina, 915 Greene St., Ste. 357, Columbia, SC 29208. Tel.: 803.777.9928; E-mail: mkhan@mailbox.sc.edu.

DISCLOSURES

No external funding was received for this work. The authors have no conflicts of interest to report.

Study concept and design were contributed by Lee, along with Khan and Salloum. Lee collected the data, and data interpretation was performed by Lee, Khan, and Salloum. The manuscript was written primarily by Lee, with assistance from Khan and Salloum, and revised by Lee, Khan, and Salloum.

REFERENCES

- Schumock GT, Li EC, Suda KJ, et al. National trends in prescription drug expenditures and projections for 2014. *Am J Health Syst Pharm*. 2014;71(6):482-99.
- Zivin K, Ratliff S, Heisler MM, Langa KM, Piette JD. Factors influencing cost-related nonadherence to medication in older adults: a conceptually based approach. *Value Health*. 2010;13(4):338-45.
- Bender E. Seeking value as cancer drug costs soar. *Cancer Discov*. 2013;3(8):833-34.
- Tamblyn R, Laprise R, Hanley JA, et al. Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA*. 2001;285(4):421-29.
- Bambauer KZ, Safran DG, Ross-Degnan D, et al. Depression and cost-related medication nonadherence in Medicare beneficiaries. *Arch Gen Psychiatry*. 2007;64(5):602-08.
- Langa KM, Fendrick AM, Chernew ME, Kabeto MU, Paisley KL, Hayman JA. Out-of-pocket health-care expenditures among older Americans with cancer. *Value Health*. 2004;7(2):186-94.
- Davidoff AJ, Erten M, Shaffer T, et al. Out-of-pocket health care expenditure burden for Medicare beneficiaries with cancer. *Cancer*. 2013;119(6):1257-65.
- Pezzin LE, O'Neil MB, Nattinger AB. The economic consequences of breast cancer adjuvant hormonal treatments. *J Gen Intern Med*. 2009;24(Suppl 2):S446-50.
- Kent EE, Forsythe LP, Yabroff KR, et al. Are survivors who report cancer-related financial problems more likely to forgo or delay medical care? *Cancer*. 2013;119(20):3710-17.
- Lee M, Khan MM. Gender differences in cost-related medication non-adherence among cancer survivors. *J Cancer Surviv*. 2016;10(2):384-93.
- Lee M, Salloum RG. Racial and ethnic disparities in cost-related medication non-adherence among cancer survivors. *J Cancer Surviv*. 2016;10(3):534-44.
- Nekhlyudov L, Madden J, Graves AJ, Zhang F, Soumerai SB, Ross-Degnan D. Cost-related medication nonadherence and cost-saving strategies used by elderly Medicare cancer survivors. *J Cancer Surviv*. 2011;5(4):395-404.
- Sabatino SA, Coates RJ, Uhler RJ, Alley LG, Pollack LA. Health insurance coverage and cost barriers to needed medical care among U.S. adult cancer survivors age < 65 years. *Cancer*. 2006;106(11):2466-75.
- Thorpe KE, Howard D. Health insurance and spending among cancer patients. *Health Aff (Millwood)*. 2003 Jan-Jun;Suppl Web Exclusives: W3-189-198. Available at: https://pdflegend.com/download/health-insurance-and-spending-among-cancer-patients-_59fa32afd64ab23ff0cac129_.pdf. Accessed December 3, 2017.
- Riley GF, Warren JL, Harlan LC, Blackwell SA. Endocrine therapy use among elderly hormone receptor-positive breast cancer patients enrolled in Medicare Part D. *Medicare Medicaid Res Rev*. 2011;1(4).
- Adams PF, Kirzinger WK, Martinez ME. Summary health statistics for the U.S. population: National Health Interview Survey, 2011. *Vital Health Stat* 10. 2012;(255):1-110.
- Adams PF, Kirzinger WK, Martinez M. Summary health statistics for the U.S. population: National Health Interview Survey, 2012. *Vital Health Stat* 10. 2013;(259):1-95.
- Parsons VL, Moriarity C, Jonas K, Moore TF, Davis KE, Tompkins L. Design and estimation for the National Health Interview Survey, 2006-2015. *Vital Health Stat* 2. 2014;(165):1-53.
- Bleyer A, Budd T, Montello M. Adolescents and young adults with cancer: the scope of the problem and criticality of clinical trials. *Cancer*. 2006;107(7 Suppl):1645-55.
- Kirchhoff AC, Lyles CR, Fluchel M, Wright J, Leisenring W. Limitations in health care access and utilization among long-term survivors of adolescent and young adult cancer. *Cancer*. 2012;118(23):5964-72.
- Weaver KE, Rowland JH, Bellizzi KM, Aziz NM. Forgoing medical care because of cost: assessing disparities in healthcare access among cancer survivors living in the United States. *Cancer*. 2010;116(14):3493-504.
- Yin W, Basu A, Zhang JX, Rabbani A, Meltzer DO, Alexander GC. The effect of the Medicare Part D prescription benefit on drug utilization and expenditures. *Ann Intern Med*. 2008;148(3):169-77.