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Research article

Age and Stage Effects on The Initial Costs of Cancer- Analysis from Population-based and Patient-Level Data

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Abstract

Background: Health care costs for cancer are substantial and expected to increase significantly in the future throughout the world. Individual patient-level costs provide insights into the intensity and patterns of care, while the treatment costs for cancer based on its stage upon diagnosis help quantify the gains from early detection. Most studies in the literature on this topic have focused on the age cohort of 65 years and older, but treatment may differ for the younger population. Linking cancer registry with National Health Insurance (NHI) claims data presents a better picture regarding the costs and treatment patterns of cancer care by age and stage. Methods: The study merges three administrative datasets in Taiwan: cancer registry, NHI claims, and underwriting data. Six cancer sites and four age groups (15-44, 45-64, 65-74, 75 and older) are investigated, log-linear models for the initial costs are constructed, and treatment rates by site, stage, and age are calculated. Results: The Charlson comorbidity index significantly correlates with higher costs. Patients aged 65-74 and 75 and older incur notably lower costs than patients aged 45-64 for various cancers at different stages. The surgical rate generally decreases with advancement of the cancer stage, while chemotherapy rates increase with such advancement. Conclusions: The more advanced the stage is, the higher the costs will be. For those at the same stage of cancer, lower treatment rates and lower costs are found for older patients. Moreover, "Younger patients have a higher proportion of later-stage cancer" only occurs for female breast cancer.

Keywords: administrative data, cancer, health care costs, initial costs, national health insurance

Introduction

The number of patients with cancer is continuously rising around the world due to its increasing incidences and the greater number of survivals. As a result, health care costs are substantial and expected to grow significantly in the future for many countries [1,2]. Individual patient-level costs provide insights into the intensity and patterns of care and allow researchers to compare the financial impacts of alternative payment models. Moreover, the treatment costs based upon the cancer stage upon diagnosis are important for quantifying the gains from early detection, thus reflecting the cost-effectiveness of treatment or preventative interventions [3].

Linking together the Surveillance, Epidemiology and End Results (SEER) database and Medicare claims records has given researchers a great opportunity to better estimate the economic costs of cancer in the U.S., thus opening up a new door for policy analyses, especially on the health care costs of cancer [4-11]. While most research has focused on the population 65 years and older, treatment may differ in younger populations [2,12-14]. Utilizing databases that cover all age groups and are nationally-representative samples (or even national population) should be a better alternative for providing a fuller picture about cancer's health care costs.

Materials and Methods

Taiwan implemented its own National Health Insurance (NHI) in 1995. It is a government-administered, integrated social insurance scheme (a single-payer system). It offers comprehensive benefits coverage for more than 99% of the people living in Taiwan, and patients are free to choose providers whenever in need. The benefits include inpatient services, outpatient services, home care, hospice care, and drugs under very low cost-sharing. For major diseases including cancer, cost-sharing is even waived.

We use three administrative datasets in this study for analysis: Taiwan cancer registry, NHI claims, and underwriting data; all of them cover the whole population of Taiwan. The cancer registry started in 1979, as hospitals with 50 or more beds are required to report cancer cases (invasive as well as in situ cancers) to the Health Promotion Administration, Ministry of Health and Welfare. Data checking and correction have been done regularly, and its quality has gained an international reputation over the years [15]. It provides information on the characteristics of newly-diagnosed cancer patients, including date of diagnosis, cancer site, and cancer stage using the American Joint Committee on Cancer (AJCC) definitions (the dataset used in this study is the 6th edition); it also includes the first time of treatment, such as whether the patient has received surgery, radiotherapy, and/or chemotherapy after diagnosis. NHI claims data present information on dates and types of health care utilization and their associated costs, whereas NHI underwriting data present information on the characteristics of the insured, including date of birth, gender, and area of residence. All these datasets are linked by a unique scrambled personal identification number.

The analysis herein includes those primary diagnoses (ICD9-CM codes) of the health care services that are cancer-related. Area of residence is defined by the 6 regions where NHI branch offices are located. Six cancer sites are investigated separately, with four commonly studied in the past literature: colorectal, female breast, lung, and prostate cancers; two are specific to Taiwan: liver and oral cancers. Four age groups are distinguished: 15-44, 45-64, 65-74 and 75 and older.

In order to know how the advancement of cancer stage affects the initial costs (health care costs for the first 6 months immediately following diagnosis) and whether there are any differences related to the age of the patient, we construct a site-specific regression model with the dependent variable being the log of the initial costs, adjusted for CPI, for each patient. The independent variables include patient's gender, stage of cancer, interaction of stage and age, Charlson comorbidity index, and area of residence.

Since the cancer registry is available up to 2013 at the time of this study, and together with the target of having enough cases for each cell, we use newly-diagnosed cancer patients in 2012 and 2013 (with their claims data from 2011 to 2014) as the sample observations. The analysis employs software SAS9.4, and the significance level is at 5%. The Charlson comorbidity index is calculated using the ICD9-CM codes from both inpatient and outpatient utilizations for one year prior to the date of diagnosis together with outpatient utilizations 3 months after the date of diagnosis in order to include diagnosed chronic conditions that were detected as part of the diagnostic workup for the cancer. We further calculate the treatment (surgery, radiotherapy and chemotherapy) rates by site, stage, and age groups as well as the statistical significance level, which we generate by using the difference between two means, with patients aged 45-64 taken as the reference.

Results

For the four types of cancers that are prevalent in both sexes, males have a higher proportion in all of them. The elderly occupies a higher proportion than non-elderly for colorectal, liver, lung, and prostate cancers (Table 1). The stage distribution within each age group further shows that those aged 15-44 have a higher percentage at stages III and IV than those aged 45-64 for colorectal cancer (43.3% vs. 35.9%) and liver cancer (41.1% vs. 35.2%), but a lower percentage for female breast (10.6% vs. 11.4%), lung cancer (60.2% vs. 64.8%), and oral cancer (48.7% vs. 53.3%). Moreover, those aged 75 and older always have a higher percentage at stages III and IV than those aged 65-74 for all cancers studied; they are 41.7% vs. 36.0% for colorectal cancer, 20.1% vs. 13.2% for female breast cancer, 35.8% vs. 32.4% for liver cancer, 71.8% vs. 68.7% for lung cancer, 51.2% vs. 49.8% for oral cancer, and 42.3% vs. 36.3% for prostate cancer. In general, patients with female breast cancer have higher percentages at the lower stage of cancer, while patients with lung cancer have higher percentages at the higher stage, regardless of age groups.

Comparing the treatment rates (the percentage of patients with a particular type of treatment) for those aged 15-44 with those aged 45-64 (the reference group), we find several statistically significant differences that are more positive (14 cases) than negative (3 cases). For example, a significantly positive difference appears in the chemotherapy rates for colorectal cancer at stage II to stage IV; for female breast cancer at stages 0, I, and IV; in radiotherapy rates for female breast cancer at stages I and II; and in surgical rates for oral cancer at stage II to stage IV. A significantly negative difference appears in the radiotherapy rate for colorectal cancer and for oral cancer at stage I; and in the chemotherapy rate for lung cancer at stage 0 (Supplementary table 1).

A comparison of the treatment rates between those aged 65-74 and those aged 45-64 displays a much clearer picture: more significant differences are found and nearly all are significantly negative differences. In addition, those aged 75 and older almost always have significantly lower surgical, radiotherapy, and chemotherapy rates than those aged 45-64 and those aged 65-74, regardless of cancer sites and for almost all cancer stages.

The log-linear regression results of the initial costs for each patient show that the Charlson comorbidity index significantly positively correlates with the costs of all six cancers studied. For those cancers prevalent in both sexes, the costs for male are significantly higher versus females for liver and oral cancers, but not significant for colorectal and lung cancers. In addition, as the cancer stage advances, the costs are significantly higher: compared to the costs in stage II, the costs are significantly higher at stages III and IV and significantly lower at stages 0 and I (Table 2).

In regard to the impacts of the interaction between stages (stage 0, stage I, stage II, stage III, and stage IV) and age groups (15-44, 65-74, and 75 and older versus 45-64) on the initial costs, the regression results show that after controlling for the stage, those aged 75 and older have significantly lower costs than those aged 45-64 for all cancers at stages I to IV, except for oral cancer at stage I and prostate cancer at stage III (which has lower costs, but they are not statistically significant); those aged 65-74 have significantly lower costs than those aged 45-64 for colorectal cancer at stage IV, for female breast cancer at stages I and II, for liver cancer at stages II and III, for lung cancer at stages III and IV, and for prostate cancer at stages I and IV. Though the cost differences between those aged 15-44 and those aged 45-64 are generally positive, only the differences for female breast cancer patients at stage II and liver cancer patients at stage III are statistically significant.

Discussion and Conclusions

Within the total economic costs of cancer, the share of direct medical care costs has gone up in many countries, with new treatments and higher incidences caused by aging populations being the important driving forces [16,17]. Since population-based and patient-level cost data for cancer as well as the cancer registry are not readily available, past researchers can only conduct limited cost analyses for cancer at the population and patient levels. For example, the majority of related articles in the U.S. have used the SEER database linked with Medicare claims; [18] in which Medicare covers primarily those 65 years and older. Some studies have covered the younger population, but just for a particular state or a particular hospital: one study linked North Carolina's cancer registry and Medicaid claims; [18] another linked North Carolina's cancer registry and private insurers' enrollment files; [19] and one employed hospital-based cancer registry and cost data [20].

Two population-based studies have appeared in the literature recently, but their costs are either assigned to the patient level or disaggregated to a broader base. Merging the cancer registry with the NHI database is thus a better alternative. As far as we know, one study has used such a data file, and it covered around 80% of the population and used the reimbursements paid to the patients [21]. By linking the cancer registry with Taiwan's NHI, we are able to identify newly-diagnosed cancer patients and obtain their health care utilization and associated costs, thus forming population-based patient-level data. With this kind of data, we can then study all related issues in one setting.

Health care costs are usually defined according to the period from diagnosis to death. Three phases (initial, continuing, and final care) are commonly used, with the costs curve being U-shaped [2,4-6,8,9,20,22-24]. Since the initial costs often provide insights into the intensity and patterns of treatment, it is therefore very important to know the magnitude of the costs and their influential factors. Each patient's age, gender, social economic status (taking the area of residence as a proxy), gen-

Table 1. Patient characteristics for selected cancer sites

Variable \ Cancer Site	**Colorectal**	**Female Breast**	**Liver**	**Lung**	**Oral**	**Prostate**
Newly-diagnosed in	29533	23419	20047	20371	12508	8594
2012 & 2013						
Gender (%)						
Male	57.5	0	69.4	59.3	91	100
Female	42.5	100	39.6	40.7	9	0
Age and Stage (N; %)						
15-44	1804	4442	1142	839	2037	
0	1.4	11.2	0	1	0	
I	12.4	24.5	27.2	17.5	19.1	
II	8.9	35.2	11.4	4.8	15.2	
III	24.6	6.6	24.9	10	11.4	
IV	18.7	4	16.2	50.2	37.3	
unknown	33.9	18.1	20.3	16.6	17	
45-64	12167	14629	8401	7481	7919	1572
0	3.3	15.1	0	0.3	0	0.2
I	16	27.7	32.7	18.4	17.4	15.6
II	10.3	29.4	16.8	4	15	38.3
III	21.4	6.5	20.5	14	11.6	11.3
IV	14.5	4.9	14.7	50.8	41.7	21.2
unknown	34.6	16.4	15.4	12.6	14.4	13.4
65-74	7005	2904	5288	5045	1630	2999
0	3.1	10.7	0	0.2	0	0.1
I	16.8	27.6	34.2	14.7	19.9	12
II	12	33.7	18	4.4	17.4	37.6
III	21.6	7.7	19.2	16.4	11.5	12.7
IV	14.3	5.5	13.2	52.3	38.3	23.6
unknown	32	14.7	15.4	11.9	12.9	13.9
75 & older	8557	1444	5216	7006	922	4023
0	2	6.3	0	0.1	0	0.2
I	12.2	17.7	28.1	9.2	16.6	7.1
II	16.3	40.6	15.8	4.3	17.7	31
III	23.4	11.3	22	14.6	9.7	11.5
IV	18.3	8.8	13.8	57.2	41.5	30.8
unknown	27.8	15.4	20.3	14.6	14.5	19.4

Table2. Regression results for the initial costs of selected cancer sites

	Colorectal		**Female Breast**		**Liver**		**Lung**		**Oral**		**Prostate**	
	Coef.	**p value**	**Coef.**	**p value**	**Coef.**	**p value**	**Coef.**	**p value**	**Coef.**	**p value**	**Coef.**	**p value**
Intercept	11.5377	<.0001	11.6696	<.0001	10.6524	<.0001	12.1366	<.0001	12.1006	<.0001	11.0746	<.0001
Gender												
Male	-0.0056	0.8227			0.1148	0.0011	-0.0152	0.5132	0.1331	0.0021		
Stage												
0	-1.9276	<.0001	-0.257	<.0001			-0.5049	0.1284				
I	-0.3916	<.0001	-0.0236	0.3917	0.0632	0.38	-0.4605	<.0001	-0.6261	<.0001	-0.3771	0.0168
III	0.0945	0.1804	0.1521	0.0007	0.6537	<.0001	0.1067	0.3013	0.2917	<.0001	0.394	0.0256
IV	0.0901	0.2399	0.1373	0.0081	0.7548	<.0001	-0.1698	0.735	0.4046	<.0001	0.0657	0.6452
Other	-2.0203	<.0001	-0.458	<.0001	0.1371	0.1084	-0.5787	<.0001	-0.597	<.0001	-0.5032	0.0027
Stage = 0												
Age15-44	0.822	0.0532	0.0298	0.6292			0.1321	0.8361				
Age 65-74	-0.0373	0.8396	-0.2669	0.0005			0.2744	0.6297				
Age 75 & older	-0.196	0.331	-1.0109	<.0001			0.19	0.7901				
Stage = I												
Age15-44	-0.3081	0.0358	0.0596	0.1647	0.0816	0.5362	-0.2605	0.0564	0.0096	0.9022	-3.4972	0.0035
Age 65-74	-0.0229	0.7649	-0.1927	<.0001	-0.1144	0.0851	0.118	0.0989	-0.0234	0.7793	-0.5263	0.0023
Age 75 & older	-0.2659	0.0009	-0.695	<.0001	-0.6062	<.0001	-0.2762	0.0002	-0.1145	0.3235	-0.9583	<.0001
Stage = II												
Age15-44	0.1883	0.2733	0.0875	0.0185	-0.732	0.0003	-0.1999	0.4479	-0.0242	0.7792	-3.2416	0.0017
Age 65-74	-0.1274	0.1644	-0.2246	<.0001	-0.2517	0.0064	-0.2497	0.0727	-0.0842	0.3472	-0.0204	0.8461
Age 75 & older	-0.4218	<.0001	-0.6909	<.0001	-0.4711	<.0001	-0.7969	<.0001	-0.3754	0.0009	-0.3486	0.0008
Stage = III												
Age15-44	0.0585	0.5788	0.107	0.2009	0.3886	0.0062	0.0633	0.7225	-0.0145	0.8842		.
Age 65-74	-0.1115	0.0941	-0.1154	0.2158	-0.2677	0.0022	-0.2156	0.0033	-0.105	0.333	0.036	0.8479
Age 75 & older	-0.4576	<.0001	-0.61	<.0001	-0.7965	<.0001	-0.8327	<.0001	-0.676	<.0001	-0.3053	0.0953

Notes: Females at stage II and living in the central area are the reference group; and for each particular stage, those at age 45-64 are the reference group.

Table 3. Regression results for the initial costs of selected cancer sites (cont'd)

	Colorectal		Female Breast		Liver		Lung		Oral		Prostate	
	Coef.	p value	Coef.	p value	Coef.	p value	Coef.	p value	Coef.	p value	Coef.	p value
Stage = IV												
Age15-44	0.1596	0.1952	0.1646	0.1197	0.1431	0.41	0.1137	0.1615	0.1023	0.0601		
Age 65-74	-0.2455	0.0029	-0.0434	0.6958	-0.1489	0.153	-0.2021	<.0001	-0.075	0.204	-0.368	0.0077
Age 75 & older	-0.6559	<.0001	-0.8137	<.0001	-0.6883	<.0001	-0.7095	<.0001	-0.638	<.0001	-0.668	<.0001
Stage = V												
Age15-44	0.3795	<.0001	0.266	<.0001	0.2793	0.082	0.1014	0.4762	0.0232	0.7811	0.8343	0.5685
Age 65-74	0.2395	<.0001	-0.1765	0.0081	-0.2243	0.024	-0.1375	0.0994	-0.368	0.0003	-0.176	0.3208
Age 75 & older	0.4388	<.0001	-1.0361	<.0001	-0.9493	<.0001	-1.0815	<.0001	-0.704	<.0001	-0.485	0.0032
Comorbidity Index	0.1119	<.0001	0.1181	<.0001	0.0395	<.0001	0.051	<.0001	0.0651	<.0001	0.1064	<.0001
Area of residence												
Taipei area	0.0394	0.2781	-0.0482	0.0411	0.2568	<.0001	0.0762	0.0189	-0.041	0.2547	0.034	0.5966
Northern area	0.1205	0.0076	-0.0679	0.0242	0.0631	0.287	-0.0013	0.9747	-0.007	0.8736	-0.025	0.7609
Southern area	0.0395	0.3481	-0.0784	0.0098	-0.003	0.952	-0.0376	0.3207	-0.012	0.7636	-0.182	0.0214
Kaoping area	-0.0034	0.9363	-0.1989	<.0001	0.0898	0.078	-0.0484	0.206	-0.204	<.0001	-0.02	0.7912
Eastern area	0.1813	0.0361	-0.1244	0.0457	0.2458	0.021	-0.0321	0.6679	-0.069	0.3035	0.1385	0.3621
R^2	0.1567		0.0681		0.0438		0.0638		0.1181		0.0461	

eral health condition (using the Charlson comorbidity index as a proxy), and disease severity (stage at diagnosis) are therefore included in the cost model.

The results of the site-specific cost model show that a higher Charlson comorbidity index is associated with significantly higher costs, and that costs for males are significantly higher than for females. Both findings are in line with previous research results, because more resources are used for patients with a higher number of comorbidities, and women are less likely to undergo surgery at the time of diagnosis [25,26]. Moreover, as the stage of cancer advances, the costs are generally significantly higher [3]. Therefore, the stage upon diagnosis is an important predictor of treatment costs, because the more advanced the disease is, the more intensive or invasive the treatment will be [27,28].

The impact of the interaction term for stage and age further indicates that for those at the same stage of cancer, patients aged 75 and older incur significantly less costs than patients aged 45-64 for all six cancers at almost all stages. Patients aged 65-74 incur significantly lower costs than patients aged 45-64 for certain cancers at specific stages: for example, for colorectal cancer at stage IV and for lung cancer at stages III and IV, but none for oral cancer. Patients aged 15-44 incur significantly higher costs than patients aged 45-64 for female breast cancer at stage II and for liver cancer at stage III (Table 3). These results echo the significantly higher radiotherapy rate for female breast cancer at stage II and significantly higher surgical and chemotherapy rates for liver cancer at stage III (Supplementary table 1). However, the significantly higher radiotherapy and chemotherapy rates for female breast cancer at stage I and significantly higher surgical rate for oral cancer at stages II to IV, shown in Supplementary table 1, are not reflected in the coefficients of the cost model. Though the treatments comprise the major portion of the costs, the above implies that for other factors such as the type, or the intensity of the use of chemotherapy, or the levels of radiotherapy, the information not available in the dataset also influence the costs [14].

Since past research on the medical costs of cancer for younger patients primarily focused on female breast cancer, we therefore discuss our results with the previous results in this regard. The study that linked North Carolina's cancer registry 2003 to 2010 to claims data from private insurers found for younger women (aged 21-44) that AJCC 6th edition stage I cancer was 34%, stage II was 40%, and stages III/IV was 16%; for older women (aged 45-64) the corresponding figures were 46%, 34%, and 12%, respectively. They therefore drew the conclusion that younger patients have a higher proportion of later-stage cancer and also showed that younger women have higher within stage excess costs, especially for stage I [19]. Another study that linked North Carolina's cancer registry 2003 to 2008 with Medicaid enrollment had the same findings: younger patients (18-44) had a higher prevalence of late-stage cancer than older women (45-64) on Medicaid, and younger patients had higher within-stage costs [18]. The diagnosis of female breast cancer is often delayed, thus resulting in a more advanced

In our study, younger women (aged 15-44) with female breast cancer at stage I occupied 35.7%, 35.2% were stage II, and 10.6% were stage III/IV; for older women (aged 45-64) the corresponding figures were 42.8%, 29.4%, and 11.4%, respectively. While younger patients with a higher proportion of later-stage cancer hold true in our study, other cancers studied do not exhibit the same results. In addition, the cost differential between younger and older female patients with breast cancer is only statistically significant for stage II, but not for stage I. Since the costs incurred for treating the cancer depend upon the delivery system as well as the payment scheme, the different costs should not be a total surprise.

The treatment patterns differ among cancer sites due to varied contemporary therapies for each site. The treatment rates by site, stage, and age demonstrate that regardless of the cancer sites and for almost all stages, non-elderly patients have significantly higher surgical rates than elderly patients and also have significantly higher radiotherapy and chemotherapy rates, and therefore they incur significantly higher costs than the elderly. Moreover, the surgical rate generally decreases with advancement of the cancer stage [2], while chemotherapy rates increase with advancement of the stage, since upon late-stage diagnosis, surgery often is not possible, which leaves chemotherapy as the patient's only option [30].

The above results are consistent with other studies. For example, older cancer patients may receive less aggressive care, as seen by less chemotherapy used in the elderly [31]. Conversely, patients under the age of 65 receive more aggressive care and have higher health care costs than older cancer patients [2,12-14].

Aside from cancer characteristics and patient attributes, the payment system is also influential in determining health care costs. The hospital global budget scheme in Taiwan is a unique system from the global perspective. All hospitals are subject to a single budget, unlike a hospital-specific global budget that is often adopted elsewhere. The strong cost containment power of Taiwan's NHI promotes the efficiency of the delivery system.

The country's NHI collects premiums according to the insured's ability to pay and then pays for the health care costs according to the insured's health care needs, as reflected by the health care claims. Therefore, in the cost model of this study the area of residence does not reflect the social economic status of the residence, but rather the health services rendered to the residents. The cost differential by area of residence thus reflects the effectiveness of the delivery systems in various areas [32].

From various databases we notice that more and more young people are getting cancer, not only in Taiwan, but also in other countries as well. For example, the incidence rates for both colon and rectal cancers declined among adults 55 years of age and older in U.S. between 2005 to 2014, but they increased annually by 1.4% and 2.4% respectively among those younger than age 55 [33]. Nevertheless, the elderly still dominate in overall numbers.

In sum, most studies in the literature on the health care costs of cancer have focused on the age cohort of 65 years and older due to data availability. Linking three administrative datasets in Taiwan - cancer registry, NHI claims, and underwriting data - this study investigates the health care costs for four age groups (15-44, 45-64, 65-74, 75 and older) and six common cancer sites, thus providing a fuller picture about cancer's health care costs.

Since there is no a priori information regarding the stage distribution within each age group in the literature, except for female breast cancer, the study offers no discussion in this regard.

However, screening for colorectal cancer has been emphasized and successfully implemented in recent years, thus resulting in a higher share of early stage colorectal cancer in the elderly.

A comparison of treatment rates between age groups displays that those aged 75 and older almost always have significantly lower surgical, radiotherapy, and chemotherapy rates than those aged 45-64 and those aged 65-74, regardless of cancer sites and for almost all cancer stages.

The site-specific log-linear models for the initial costs further show that the Charlson comorbidity index significantly correlates to higher costs and the costs for male are significantly higher than for females. The impact of the interaction term for stage and age further indicates that for those at the same stage of cancer, patients aged 75 and older incur significantly less costs than patients aged 45-64 for all six cancers at almost all stages. Patients aged 65-74 have significantly lower costs than patients aged 45-64 for certain cancers at specific stages. Therefore, health care resources are generally efficiently used for cancer.

This study does have some limitations. First, the health care costs analyzed herein are insurance claims rather than charges to the patients, and therefore benefits that are not covered by NHI are not included. Second, the health care costs for cancer are influenced not only by patient demographics and cancer characteristics, but also by the delivery system and payment scheme. Thus, what we have presented in this study may not be directly applicable to another country or another health care system. However, since we have investigated the treatment patterns and the initial costs for six common cancers and four age groups in one setting, readers can look at the issue from broader spectrum. Third, the site-specific cost differentials by area of residence do not show similar patterns across the site, implying that an area's health resources play an important role. Since the focus of this study is more on patient characteristics and disease severity, the empirical results regarding the cost differentials by area of residence are not discussed, but offer a future issue for investigation.

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