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Insurance Status and Other Non-biological Factors Predict Outcomes in Acute Myelogenous Leukemia: Analysis of Data from the National Cancer Database

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Abstract. *Background: The treatment of acute myeloid leukemia (AML) has made significant progress in the last 30 years; however, numerous factors affect outcomes in patients with AML. Well-known risk factors are age, cytogenetics, and treatment intensity. The purpose of our study was to investigate the effects of insurance status on the outcome of AML; age, Carlson comorbidity index, distance travelled to the treatment center, and type of treatment center were adjusted by analyzing data from National Cancer Database (NCDB). In the wake of the Affordable Care Act, and its impact on insurance coverage, evaluating the effect having insurance has on health outcome is urgently necessary. Materials and Methods: Data were analyzed from 67,443 men and women (≥18 years of age), who were registered in the NCDB and diagnosed with AML between 1998 and 2011 with follow-up to the end of 2012. The primary predictor variable was payer status, and the outcome variable was overall survival. Additional variables addressed and adjusted, included: sex, age, race, Charleston Comorbidity index, level of education, income, distance traveled, facility type, diagnosing/treating facility, treatment delay, and chemotherapy. Results: In multivariate analysis, after adjusting for other predictor variables, payer status was a statistically significant predictor of overall survival for AML. Relative to privately insured patients, patients with Medicaid had a 17% increased risk, those without insurance had a 21% increased risk, those with Medicare had a 19% increased risk and those with unknown insurance status had a 22% increased risk of mortality from AML. The percentage of patients surviving from AML after 24 months was 37.6%, 31.4%, 32.3%, 31.8%, and 33.1% for patients with private, unknown, Medicare, uninsured, and Medicaid payer status, respectively. All factors investigated were found to be significant predictors of AML survival except distance traveled. Conclusion: We observed that payer status has a statistically significant relationship with overall survival from AML.*

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The American Cancer Society estimates there will be about 19,950 new cases and 10,430 deaths from acute myeloid leukemia (AML) in 2016, of which most will affect adults (1). AML is typically an older person's disease, being uncommon before the age of 45 years. In 2008, the World Health Organization (WHO) revised the classification of AML for proper prognostication based on morphology, immunophenotyping, cytogenetic data, and molecular studies (2, 3). AML is also divided based on risk into high, intermediate, and low groups (4-7). Recently Arber *et al.* published the latest classification of AML based on new clinical, prognostic, morphological, immunophenotypic, and genetic data (8).

Complete remission (CR) rates in older adults with AML are 40-60% with treatment (9-18). The 5-year survival rate has increased from 6.3% in 1975 to 23.9% in 2007 according to Surveillance, Epidemiology and End result program (SEER) data analysis. Overall survival rates for AML decrease as age increases (19). Older adults are also more likely to have comorbidities and poorer performance status. This increases treatment-related morbidity and mortality, and limits intensive treatments such as allogenic hematopoietic cell transplantation.

There exist many risk factors associated with survival of patients with AML. Well-known risk factors are age, cytogenetics, molecular markers, and treatment intensity. Other factors, including access to healthcare, modify treatment outcomes. For example, the type of insurance a patient has might influence the cancer treatment outcome.

Previous studies on solid tumors have identified a link between uninsured and underinsured payer status and shorter survival from several cancer types (20-25). However, this relationship has not been demonstrated in patients with AML in whom disease progression is certain, and in the absence of treatment, prognosis is almost always death. Bradley *et al*. demonstrated uninsured patients were 4.4 times more likely to be untreated than their privately insured counterparts and had a 29% higher likelihood of death. Once treatment was adjusted in the survival analyses, differences between insurance groups were not statistically significant (26). These findings demonstrate the critical role of health insurance in AML, which is a life-threatening disease that is expensive to treat (26-28).

As healthcare reform in the United States continues to evolve, it is challenging to define the impact of payer status on health outcomes. In the infancy of the Affordable Care Act, many expect a more comprehensive coverage will improve outcomes across the United States (29-33). Yet the effect that this shift will have on patients with cancer is still uncertain.

The National Cancer Data Base (NCDB) began collecting information on payer status for all patients in 1996. This dataset provides the opportunity to examine the relationship between payer status and overall survival of patients with cancer. Recent studies using these data found a statistically significant relationship between payer status and survival from breast, colon, and lung cancer (34-36). The impact of payer status on outcomes of AML is unknown. In an analysis of 67,433 patients with AML from the NCDB, we assessed here how payer status affects survival in AML, adjusting for age, comorbidity index, distance travelled from, and type of treatment center.

Materials and Methods

This study examined data regarding 67,443 patients who were diagnosed with AML between 1998 and 2011 and followed-up until December 31, 2012, and they were registered in the de-identified NCDB. Only patients who had complete survival data and complete chemotherapy data (no, single, multiple agent) were included in the analysis. The NCDB captures approximately 70% of all newly diagnosed cases of cancer in the United States at the institutional level. (37) The International Classification of Disease for Oncology, third edition (ICD-O-3), codes (C420, C421, C424) for a diagnosis of AML were used to select patients. The code C420, C421 and C424 represent blood, bone marrow and hematopoetic not otherwise specified. Then we used histological codes 9840, 9861, 9865-9867, 9869, 9871-9874, 9895-9897, 9898, 9910-9911, 9920 for AML.

The outcome variable of overall survival was calculated from date of diagnosis to date of death, date of loss to follow-up, or date of study end (December 31, 2012). The primary predictor variable of payer status was categorized as uninsured, private, Medicaid, Medicare, or unknown. Other variables investigated included sex, age, race, Charlson Comorbidity index, income, education, distance traveled to treating facility, facility type, diagnosing/treating facility, treatment delay, and chemotherapy. Age was grouped as 18-49, 50-64, 65-74, or ≥75 years. Race was categorized as White, Black, or Asian. Charlson Comorbidity Index, a score that indicates the overall health status of a patient, was defined as 0, 1, ≥2, or unknown (38). Income, or median household income at zip code level, was grouped as <$30, $30-34, $35-45, or ≥$46 k. Education measured as the percentage of adults in the patient's zip code who did not graduate from high school was grouped as <14%, 14-19.9%, 20-28.9%, and ≥29%. Education was determined using the 2000 census data. Distance traveled, *i.e*. the distance from the patient's residential zip code to a medical center, was defined as <30 or ≥30 miles. Facility type was categorized as a community cancer program, a comprehensive cancer program, or an academic or research cancer program. Diagnosing/treating facility was categorized as either the same (diagnosed and treated at the same facility) or different (diagnosed at one facility and treated at another). Treatment delay was grouped as 0-7, 8-30, or ≥31 days. Chemotherapy was categorized as single agent, multiple agents, or not received.

Descriptive statistics are presented for each variable studied. Multivariate Cox regression was used to simultaneously estimate the hazard of death [hazard ratio (HR)) by payer status while adjusting for other factors. Direct adjusted overall survival (OS) was calculated by using Multivariate Cox regression. Statistical Software SAS 9.4 (SAS Inc., Cary, NC, USA) was used for data management, statistical analysis, and modeling. 95% Confidence intervals (CIs) that did not include 1.00 were considered statistically significant at the 5% level.

Results

The demographic characteristics of the patient population are shown in Table I. A total of 67,443 patients were included in the study, 45.12% had Medicare at diagnosis, 40.41% had private insurance, 7.4% had Medicaid, 4.15% were uninsured, and 2.92% had an unknown insurance status.

The overall mean age at diagnosis was 61.1 years. At diagnosis, Medicare patients had, as expected, the highest mean age (73.6 years), while all other privately insured, Medicaid-insured, or uninsured patients had mean ages of 51.9, 44.6, and 46.9 years, respectively. The majority of patients in the study were White (88.1%). Most patients (63.12%) received multiple agent chemotherapy, although 21.49% received none at all.

Table II displays the HR and the 95% CI for each variable from multivariate Cox regression analysis. Payer status was a significant predictor of overall survival after adjusting for gender, age, race, comorbidity, income, education, distance traveled, facility type, treatment delay, diagnosing/treating facility, and chemotherapy. Relative to privately insured patients, Medicaid patients had a 16% increased risk of mortality from AML. Uninsured and Medicare patients had a 21% and a 19% increased risk of mortality, respectively. After 24 months, the percentage of patients surviving from AML was 37.66%, 31.44%, 32.23%, 31.76%, and 33.11% for private, unknown, Medicare, uninsured, and Medicaid payer status, respectively.

Multivariate analysis also revealed that female patients were 8% less likely to die than their male counterparts. Compared to the 18- to 49-year-old age group, patients aged 75 years and older were 4.14-times more likely to die. Relative to Whites,

Table I. *Patients' characteristics (37).*

Factor	Level	n	%
Gender	Male	36,531	54.17
	Female	30,912	45.83
Age, years	18-49	16,980	25.18
	50-64	17,659	26.18
	65-74	15,396	22.83
	75+	17,408	25.81
Race	White	59,410	88.09
	Black	5,985	8.87
	Asian	2,048	3.04
CCI	0	32,678	48.45
	1	8,647	12.82
	2	3,446	5.11
	Unknown	22,672	33.62
Year of diagnosis	1998-2004	34,220	44.29
	2005-2011	43,051	55.71
Insurance	Uninsured	2,800	4.15
	Private	27,252	40.41
	Medicaid	4,992	7.4
	Medicare	30,429	45.12
	Unknown	1,970	2.92
Income, $	30 k	8,800	13.78
	30-34 k	12,199	19.1
	35-45 k	18,198	28.49
	>46 k	24,678	38.63
Education	≥29%	11,111	17.4
	20-28.9%	14,922	23.36
	14-19.9%	15,480	24.24
	<14%	22,358	35
Distance travelled, miles	<30	47,281	72.76
	≥30	17,697	27.24
Facility type	CCP	4,761	7.06
	Comprehensive CCP	30,680	45.49
	Academic/research program	32,002	47.45
Class of case	Same facility	46,115	68.38
	Different facility	21,328	31.62
Treatment started, days from diagnosis	0-7	36,142	68.37
	8-30	12,207	23.09
	31+	4,510	8.53
Chemotherapy	None	14,494	21.49
	Single agent	10,382	15.39
	Multiple agent	42,567	63.12

CCI: Charlson Comorbidity Index; CCP: Community Cancer Program.

Table II. *Multivariate Cox regression for hazard ratio (HR) of death by factor.*

Factor	Level	HR	95% CI
Gender	Male	1.00	
	Female	0.92	0.90-0.94
Age, years	18-49	1.00	
	50-64	1.96	1.91-2.02
	65-74	2.88	2.77-2.99
	≥75	4.20	4.03-4.38
Race	White	1.00	
	Black	1.08	1.04-1.12
	Asian	0.93	0.87-0.99
CCI	0	1.00	
	1	1.24	1.20-1.28
	2	1.52	1.45-1.59
	Unknown	1.19	1.15-1.23
Year of diagnosis	1998-2004	1.00	
	2005-2011	0.86	0.83-0.88
Insurance	Private	1.00	
	Uninsured	1.20	1.14-1.27
	Medicaid	1.16	1.12-1.22
	Medicare	1.19	1.15-1.23
	Unknown	1.03	0.98-1.09
Income, $	≥46 k	1.00	
	30 k	1.10	1.06-1.15
	30-34 k	1.08	1.05-1.12
	35-45 k	1.05	1.02-1.08
Education	<14%	1.00	
	14-19.9%	1.03	1.00-1.06
	20-28.9%	1.05	1.02-1.08
	≥29%	1.01	0.97-1.05
Distance travelled, miles	≥30	1.00	
	<30	0.99	0.97-1.02
Facility type	Academic/research program	1.00	
	CCP	1.02	0.98-1.07
	Comprehensive CCP	1.04	1.02-1.06
Class of case	Same facility	1.00	
	Different facility	0.87	0.85-0.89
Treatment started, days from diagnosis	≥31	1.00	
	0-7	1.25	1.21-1.30
	8-30	1.17	1.13-1.22
Chemotherapy	None	1.00	
	Single agent	0.78	0.74-0.82
	Multiple agent	0.63	0.59-0.66

CI: Confidence interval; CCI: Charlson Comorbidity Index; CCP: Community Cancer Program.

Asians had an 8% reduced risk while Black patients had an 8% increased risk of death. Patients with two or more comorbidities were 1.49-times more likely to die than those without comorbidities. Those who received multiple agent chemotherapy had a 38% reduced risk of death as compared to those who received no chemotherapy. A finding of particular interest was that patients treated within 7 days and 8-30 days were 26% and 18% more likely to die compared to patients treated 31 days or more after diagnosis. Distance traveled was not a significant predictor of overall survival.

Discussion

Payer status has a significant effect on the overall survival of patients with AML after adjusting for all other predictive factors (see Table II). Medicare patients had a worse outcome compared to those privately insured likely due to the older age of these patients. The important comparison is between uninsured, Medicaid, and privately insured patients. Uninsured patients had worse outcomes compared to Medicaid patients, who had worse outcome compared to

private insurance. Medicaid and uninsured patients had an increased risk of dying compared to those with private insurance. Earlier studies in different types of cancer (mainly colon, breast, and lung) showed similar although not independent associations of insurance status and survival (21, 28, 34, 36, 39, 40). The mechanism by which payer status affects survival is not entirely clear; it could be mediated through differences in access to certain treatment types (41). Access to care, transportation, and supportive care may be involved. Further research and mediation analysis is needed.

Using the NCDB database of more than 60,000 patients with AML, we confirm and extend here three smaller studies about the impact of insurance on AML outcomes. Ortiz-Ortiz *et al*. described insurance-related disparities in 516 patients with leukemia in Puerto Rico (including 159 cases of AML), but did not comment on other potential confounding factors (42). Bradley *et al*. described insurance-related disparities in the Virginia Cancer Registry based on 523 patients. The highest risk of death was seen in uninsured patients (26). Borate *et al*. investigated SEER data for 5,541 patients with AML aged 19 to 64 years diagnosed between 2007 and 2011, finding an HR of death of 1.24 for Medicaid patients compared to privately insured patients using a multivariate analysis. Our data are comparable to the data of Borate *et al*. (43). Two smaller studies did not find any correlation between insurance and survival. Moreover, in a single-institutional study, no difference was found between different insurance categories, but survival was low in all categories (40). In a study from the 2002-2006 New York and California Cancer Registries, the researchers found no survival differences. However, the authors compared Medicaid patients with all other categories, including uninsured patients (44, 45).

Similar to other studies, we found patients with older age, and higher comorbidity index had the worst AML survival (9, 19). As shown in Table II, age-related mortality increases to approximately double in the 50-64 years group compared to 18-49 years. Risk of death is even higher in those aged 65 years and older, which may in part be due to the lack of chemotherapy administered.

Studies have shown that comorbidities are predictive of early death in the elderly, but not a predictor for younger patients with AML. The comorbidity index, as established in the transplant setting, is an independent predictor for early death in elderly patients (46-48). Our findings are consistent with these studies and, as demonstrated in Table II, the findings of mortality significantly increasing as the comorbidity index increased. An important question arises: Does the comorbidity index account for AML survival differences for patients with different insurance status? In a different malignancy, colon cancer, differences in comorbidity level did not account for the association between insurance status and survival (49).

An additional finding is patients treated at academic institutions had better OS compared to those treated at non-academic institutions (such as community cancer centers and comprehensive cancer centers). Patients treated at community cancer programs and comprehensive CCPs were found to have a 4-5% higher risk of dying compared to patients treated at an academic center. Similar results were observed for patients with breast cancer (50). Survival outcomes can be affected by distance travelled to treatment center. One single-center study, including 281 patients receiving induction therapy, found no association between socioeconomic status or distance from treatment center and survival. A study of a pediatric population with AML and acute lymphocytic leukemia showed distance from treatment center had no effect on outcomes in AML. Our data concurs with the other studies (51-53).

The Patient Protection and Affordable Care Act (ACA) will likely improve insurance coverage for most young adults in the United States, but some of these patients will face significant premium increase in the individual market. In a SEER data analysis of 39,447 patients aged 20 to 40 years diagnosed with a malignant neoplasm between 2007 and 2009, an association between insurance coverage and decreased likelihood of presentation with metastatic disease [odds ratio (OR), 0.84; 95% CI=0.75-0.94)] increased receipt of definitive treatment (OR=1.95; 95% CI=1.52-2.50), and reduced death resulting from any cause (HR=0.77; 95% CI=0.65-0.91) was noted. The improved coverage fostered by the ACA may translate into better outcomes among young adults with cancer. Extra consideration must be given to ensure that patients who face premium increases in the individual market can obtain insurance coverage under the ACA (54).

Despite utilizing a large sample population, there are limitations to this study. Firstly, the NCDB database does not collect information on cytogenetic or molecular subtypes of leukemia. This is important because different socioeconomic and ethnic groups may have a different biology of leukemia. Secondly, the treatment information is limited to single-agent *versus* multi-agent chemotherapy. Different patient groups may have received different treatment intensity. In particular, the NCDB database does not have detailed information about allogeneic transplantation. Allogeneic transplantation has a potential for cure; however, if used in patients with comorbidities or without good social support, transplantation may worsen the survival rate. Different insurance plans may limit access to transplantation or provide incomplete coverage for supportive care. Detailed data are not available from the NCDB on changes in treatment and change in insurance status that might have occurred over time. Thirdly, the socioeconomic status and education level is collected by zip code level not by direct patient or family information. Fourthly, the effect of factors on OS may be different from the effect on cause-specific survival.

In conclusion, insurance status is a significant predictor of OS for patients with AML. This remains true after adjusting for other previously described non-biological predictive factors. As we continue to navigate our way through the dynamically changing system of healthcare reform in the United States, it is important to consider the influence of payer status on health outcomes in future decision-making in order to mitigate disparities.

Ethics Statement

With the support from the Chair of Louisiana State University Hospital in Shreveport (currently University Health Shreveport) Cancer program, the corresponding author applied and was awarded the NCDB Participant Use Data File (PUF) for 1998 to 2011 from the Commission on Cancer. The PUF is a Health Insurance Portability and Accountability Act compliant data file containing cases submitted to the Commission on Cancer's NCDB. The PUF contains de-identified patient level data that do not identify hospitals, healthcare providers, or patients as agreed to in the Business Associate Agreement each CoC-accredited program has signed with the American College of Surgeons. The PUFs are designed to provide investigators associated with CoC-accredited cancer programs with a data resource they can use to review and advance the quality of care delivered to cancer patients through analyses of cases reported to the NCDB. NCDB PUFs are only available through an application process to investigators associated with CoC-accredited cancer programs.

Competing Interests

The Authors have no competing interests to disclose.

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References

1 ASCO statistics. http://www.cancer.net/cancer-types/leukemia-acute-myeloid-aml/statistics

2 Vardiman JW, Thiele J, Arber DA, Brunning RD, Borowitz MJ, Porwit A, Harris NL, Le Beau MM, Hellstrom-Lindberg E, Tefferi A and Bloomfield CD: The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: Rationale and important changes. Blood *114(5)*: 937-951, 2009.

3 Bennett JM: World Health Organization classification of the acute leukemias and myelodysplastic syndrome. Int J Hematol *72(2)*: 131-133, 2000.

4 Byrd JC, Mrozek K, Dodge RK, Carroll AJ, Edwards CG, Arthur DC, Pettenati MJ, Patil SR, Rao KW, Watson MS, Koduru PR, Moore JO, Stone RM, Mayer RJ, Feldman EJ, Davey FR, Schiffer CA, Larson RA, Bloomfield CD, Cancer and Leukemia Group B: Pretreatment cytogenetic abnormalities are predictive of induction success, cumulative incidence of relapse, and overall survival in adult patients with *de novo* acute myeloid leukemia: Results from Cancer and Leukemia Group B (CALGB 8461). Blood *100(13)*: 4325-4336, 2002.

5 Grimwade D, Walker H, Oliver F, Wheatley K, Harrison C, Harrison G, Rees J, Hann I, Stevens R, Burnett A and Goldstone A: The importance of diagnostic cytogenetics on outcome in AML: Analysis of 1,612 patients entered into the mrc aml 10 trial. The Medical Research Council Adult and Children's Leukaemia Working Parties. Blood *92(7)*: 2322-2333, 1998.

6 Slovak ML, Kopecky KJ, Cassileth PA, Harrington DH, Theil KS, Mohamed A, Paietta E, Willman CL, Head DR, Rowe JM, Forman SJ and Appelbaum FR: Karyotypic analysis predicts outcome of preremission and postremission therapy in adult acute myeloid leukemia: A Southwest Oncology Group/Eastern Cooperative Oncology Group study. Blood *96(13)*: 4075-4083, 2000.

7 Bienz M, Ludwig M, Leibundgut EO, Mueller BU, Ratschiller D, Solenthaler M, Fey MF and Pabst T: Risk assessment in patients with acute myeloid leukemia and a normal karyotype. Clin Cancer Res *11(4)*: 1416-1424, 2005.

8 Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, Bloomfield CD, Cazzola M and Vardiman JW: The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood *127(20)*: 2391-2405, 2016.

9 Appelbaum FR, Gundacker H, Head DR, Slovak ML, Willman CL, Godwin JE, Anderson JE and Petersdorf SH: Age and acute myeloid leukemia. Blood *107(9)*: 3481-3485, 2006.

10 Lowenberg B, Ossenkoppele GJ, van Putten W, Schouten HC, Graux C, Ferrant A, Sonneveld P, Maertens J, Jongen-Lavrencic M, von Lilienfeld-Toal M, Biemond BJ, Vellenga E, van Marwijk Kooy M, Verdonck LF, Beck J, Dohner H, Gratwohl A, Pabst T, Verhoef G, Dutch-Belgian Cooperative Trial Group for H-O, German AMLSG and Swiss Group for Clinical Cancer Research Collaborative G: High-dose daunorubicin in older patients with acute myeloid leukemia. N Engl J Med *361(13)*: 1235-1248, 2009.

11 Lowenberg B, Suciu S, Archimbaud E, Haak H, Stryckmans P, de Cataldo R, Dekker AW, Berneman ZN, Thyss A, van der Lelie J, Sonneveld P, Visani G, Fillet G, Hayat M, Hagemeijer A, Solbu G and Zittoun R: Mitoxantrone *versus* daunorubicin in induction-consolidation chemotherapy–the value of low-dose cytarabine for maintenance of remission, and an assessment of prognostic factors in acute myeloid leukemia in the elderly: Final report. European Organization for the Research and Treatment of Cancer and the Dutch-Belgian Hemato-Oncology Cooperative Hovon Group. J Clin Oncol *16(3)*: 872-881, 1998.

12 Estey E: Acute myeloid leukemia and myelodysplastic syndromes in older patients. J Clin Oncol *25(14)*: 1908-1915, 2007.

13 Ferrara F, Annunziata M, Copia C, Magrin S, Mele G and Mirto S: Therapeutic options and treatment results for patients over 75 years of age with acute myeloid leukemia. Haematologica *83(2)*: 126-131, 1998.

14 Leoni F, Ciolli S, Nozzoli C, Marrani C, Caporale R and Ferrini PR: Idarubicin in induction treatment of acute myeloid leukemia in the elderly. Haematologica *82(5 Suppl)*: 13-18, 1997.

15 Juliusson G, Hoglund M, Karlsson K, Lofgren C, Mollgard L, Paul C, Tidefelt U, Bjorkholm M and Leukemia Group of Middle Sweden: Increased remissions from one course for intermediate-dose cytosine arabinoside and idarubicin in elderly acute myeloid leukaemia when combined with cladribine. A randomized population-based phase II study. Br J Haematol *123(5)*: 810-818, 2003.

16 Vey N, Coso D, Bardou VJ, Stoppa AM, Braud AC, Bouabdallah R, Sainty D, Mozziconacci MJ, Lafage M, Damaj G, Blaise D, Gastaut JA and Maraninchi D: The benefit of induction chemotherapy in patients age > or = 75 years. Cancer *101(2)*: 325-331, 2004.

17 Gardin C, Turlure P, Fagot T, Thomas X, Terre C, Contentin N, Raffoux E, de Botton S, Pautas C, Reman O, Bourhis JH, Fenaux P, Castaigne S, Michallet M, Preudhomme C, de Revel T, Bordessoule D and Dombret H: Postremission treatment of elderly patients with acute myeloid leukemia in first complete remission after intensive induction chemotherapy: Results of the multicenter randomized Acute Leukemia French Association (ALFA) 9803 trial. Blood *109(12)*: 5129-5135, 2007.

18 British Committee for Standards in H, Milligan DW, Grimwade D, Cullis JO, Bond L, Swirsky D, Craddock C, Kell J, Homewood J, Campbell K, McGinley S, Wheatley K and Jackson G: Guidelines on the management of acute myeloid leukaemia in adults. Br J Haematol *135(4)*: 450-474, 2006.

19 Juliusson G, Antunovic P, Derolf A, Lehmann S, Mollgard L, Stockelberg D, Tidefelt U, Wahlin A and Hoglund M: Age and acute myeloid leukemia: Real world data on decision to treat and outcomes from the Swedish Acute Leukemia Registry. Blood *113(18)*: 4179-4187, 2009.

20 Yim J, Hwang SS, Yoo KY and Kim CY: Contribution of income-related inequality and healthcare utilisation to survival in cancers of the lung, liver, stomach and colon. J Epidemiol Community Health *66(1)*: 37-40, 2012.

21 Parikh AA, Robinson J, Zaydfudim VM, Penson D and Whiteside MA: The effect of health insurance status on the treatment and outcomes of patients with colorectal cancer. J Surg Oncol *110(3)*: 227-232, 2014.

22 Shi RH, Taylor H, McLarty J, Liu L, Mills G and Burton G: Effects of payer status on breast cancer survival: A retrospective study. BMC Cancer *15*: 2015.

23 Roetzheim RG, Gonzalez EC, Ferrante JM, Pal N, Van Durme DJ and Krischer JP: Effects of health insurance and race on breast carcinoma treatments and outcomes. Cancer *89(11)*: 2202-2213, 2000.

24 Shi RH, Mills G, McLarty J, Burton G, Shi ZZ and Glass J: Commercial insurance triples chances of breast cancer survival in a public hospital. Breast J *19(6)*: 664-667, 2013.

25 Wan N, Zhan FB, Lu YM and Tiefenbacher JP: Access to healthcare and disparities in colorectal cancer survival in texas. Health & Place *18(2)*: 321-329, 2012.

26 Bradley CJ, Dahman B, Jin Y, Shickle LM and Ginder GD: Acute myeloid leukemia: How the uninsured fare. Cancer *117(20)*: 4772-4778, 2011.

27 Halpern MT, Ward EM, Pavluck AL, Schrag NM, Bian J and Chen AY: Association of insurance status and ethnicity with cancer stage at diagnosis for 12 cancer sites: A retrospective analysis. Lancet Oncol *9(3)*: 222-231, 2008.

28 Ward E, Halpern M, Schrag N, Cokkinides V, DeSantis C, Bandi P, Siegel R, Stewart A and Jemal A: Association of insurance with cancer care utilization and outcomes. CA Cancer J Clin *58(1)*: 9-31, 2008.

29 Albright HW, Moreno M, Feeley TW, Walters R, Samuels M, Pereira A and Burke TW: The implications of the 2010 patient protection and affordable care act and the health care and education reconciliation act on cancer care delivery. Cancer *117(8)*: 1564-1574, 2011.

30 Brawley OW and Virgo KS: From the guest editors: Introduction for the impact of health care reform on cancer patients. Cancer J *16(6)*: 551-553, 2010.

31 Ferris LW, Farber M, Guidi TU and Laffey WJ: Impact of health care reform on the cancer patient: A view from cancer executives. Cancer J *16(6)*: 600-605, 2010.

32 Schwartz K and Claxton G: The patient protection and affordable care act: How will it affect private health insurance for cancer patients? Cancer J *16(6)*: 572-576, 2010.

33 Virgo KS, Burkhardt EA, Cokkinides VE and Ward EM: Impact of health care reform legislation on uninsured and Medicaid-insured cancer patients. Cancer J *16(6)*: 577-583, 2010.

34 Zhou X, Zhang J, Yun H, Shi R, Wang Y, Wang W, Lagercrantz SB and Mu K: Alterations of biomarker profiles after neoadjuvant chemotherapy in breast cancer: Tumor heterogeneity should be taken into consideration. Oncotarget, 2015.

35 Boland GM, Chang GJ, Haynes AB, Chiang YJ, Chagpar R, Xing Y, Hu CY, Feig BW, You YN and Cormier JN: Association between adherence to National Comprehensive Cancer Network treatment guidelines and improved survival in patients with colon cancer. Cancer *119(8)*: 1593-1601, 2013.

36 Slatore CG, Au DH, Gould MK and American Thoracic Society Disparities in Healthcare G: An official American Thoracic Society systematic review: Insurance status and disparities in lung cancer practices and outcomes. Am J Respir Crit Care Med *182(9)*: 1195-1205, 2010.

37 National Cancer Database (NCBD) https://www.facs.org/quality%20programs/cancer/ncdb

38 Charlson ME, Pompei P, Ales KL and Mackenzie CR: A new method of classifying prognostic co-morbidity in longitudinal-studies - development and validation. J Chronic Dis *40(5)*: 373-383, 1987.

39 Roetzheim RG, Pal N, Gonzalez EC, Ferrante JM, Van Durme DJ and Krischer JP: Effects of health insurance and race on colorectal cancer treatments and outcomes. Am J Public Health *90(11)*: 1746-1754, 2000.

40 Shi R, Mills G, McLarty J, Burton G, Shi Z and Glass J: Commercial insurance triples chances of breast cancer survival in a public hospital. Breast J *19(6)*: 664-667, 2013.

41 Rochon J, du Bois A and Lange T: Mediation analysis of the relationship between institutional research activity and patient survival. BMC Med Res Methodol *14*: 9, 2014.

42 Ortiz-Ortiz KJ, Ortiz-Martinez de Andino JJ, Torres-Cintron CR, Tirado-Gomez M, Gonzalez-Falero A, Caballero-Varona D, Ortiz AP and Perez-Rios N: Effect of type of health insurance coverage on leukemia survival in adults in Puerto Rico. P R Health Sci J *33(3)*: 132-135, 2014.

43 Borate UM, Mineishi S and Costa LJ: Nonbiological factors affecting survival in younger patients with acute myeloid leukemia. Cancer *121(21)*: 3877-3884, 2015.

44 Al-Ameri A, Anand A, Abdelfatah M, Kanaan Z, Hammonds T, Haller N and Cherry M: Outcome of acute myeloid leukemia and high-risk myelodysplastic syndrome according to health insurance status. Clin Lymphoma Myeloma Leuk *14(6)*: 509-513, 2014.

45 Yung RL, Chen K, Abel GA, Gesten FC, Roohan PJ, Boscoe FP, Sinclair AH, Schymura MJ and Schrag D: Cancer disparities in the context of Medicaid insurance: A comparison of survival for acute myeloid leukemia and Hodgkin's lymphoma by Medicaid enrollment. Oncologist *16(8)*: 1082-1091, 2011.

46 Charlson ME, Pompei P, Ales KL and MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis *40(5)*: 373-383, 1987.

47 Savic A, Kvrgic V, Rajic N, Urosevic I, Kovacevic D, Percic I and Popovic S: The hematopoietic cell transplantation comorbidity index is a predictor of early death and survival in adult acute myeloid leukemia patients. Leuk Res *36(4)*: 479-482, 2012.

48 Sorror ML, Giralt S, Sandmaier BM, De Lima M, Shahjahan M, Maloney DG, Deeg HJ, Appelbaum FR, Storer B and Storb R: Hematopoietic cell transplantation specific comorbidity index as an outcome predictor for patients with acute myeloid leukemia in first remission: Combined FHCRC and MDACC experiences. Blood *110(13)*: 4606-4613, 2007.

49 Robbins AS, Pavluck AL, Fedewa SA, Chen AY and Ward EM: Insurance status, comorbidity level, and survival among colorectal cancer patients age 18 to 64 years in the national cancer data base from 2003 to 2005. J Clin Oncol *27(22)*: 3627-3633, 2009.

50 Shi R, Taylor H, McLarty J, Liu L, Mills G and Burton G: Effects of payer status on breast cancer survival: A retrospective study. BMC Cancer *15*: 211, 2015.

51 Kristinsson SY, Derolf AR, Edgren G, Dickman PW and Bjorkholm M: Socioeconomic differences in patient survival are increasing for acute myeloid leukemia and multiple myeloma in Sweden. J Clin Oncol *27(12)*: 2073-2080, 2009.

52 Sergentanis T, Dessypris N, Kanavidis P, Skalkidis I, Baka M, Polychronopoulou S, Athanassiadou F, Stiakaki E, Frangandrea I, Moschovi M and Petridou ET: Socioeconomic status, area remoteness, and survival from childhood leukemia: Results from the nationwide registry for childhood hematological malignancies in Greece. Eur J Cancer Prev *22(5)*: 473-479, 2013.

53 Rodriguez CP, Baz R, Jawde RA, Rybicki LA, Kalaycio ME, Advani A, Sobecks R and Sekeres MA: Impact of socio-economic status and distance from treatment center on survival in patients receiving remission induction therapy for newly diagnosed acute myeloid leukemia. Leuk Res *32(3)*: 413-420, 2008.

54 Aizer AA, Falit B, Mendu ML, Chen MH, Choueiri TK, Hoffman KE, Hu JC, Martin NE, Trinh QD, Alexander BM and Nguyen PL: Cancer-specific outcomes among young adults without health insurance. J Clin Oncol 32(19): 2025-2030, 2014.

55 Wilensky GR: The shortfalls of "Obamacare". N Engl J Med *367(16)*: 1479-1481, 2012.

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