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## Cancer incidence in a sample of Maryland residents with serious mental illness

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### Abstract

**Objective**—Persons with serious mental illness have an increased mortality rate and a higher burden of many medical conditions compared to those without serious mental illness, but cancer risk in the serious mental illness population is uncertain. Cancer incidence in a community-based cohort of adults with schizophrenia or bipolar disorder was examined by race, sex, and cancer site.

**Methods**—We calculated standardized incidence ratios of total and site-specific cancers comparing a cohort of 3317 Maryland Medicaid adult beneficiaries with schizophrenia or bipolar disorder followed from 1994 through 2004 to the U.S. population.

**Results**—Total cancer incidence for adults with schizophrenia or bipolar disorder was 2.6 times higher than in the U.S. population. Elevated risk in persons with serious mental illness was greatest for cancer of the lung and bronchus. No differences in risk were found for African American versus white Medicaid beneficiaries with serious mental illness.

**Conclusion**—These findings suggest heightened risk for cancer among adults with schizophrenia or bipolar disorder. Clinicians should promote appropriate cancer screening and work to reduce modifiable risk factors, such as smoking, among persons with serious mental illness.

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Adults with serious mental illness have higher rates of morbidity and mortality than adults without serious mental illness, including high risk of cardiovascular disease, hypertension,

and diabetes (1-3). Although cancer is the second leading cause of death in the overall population (4), evidence varies on cancer risk among persons with serious mental illness. Due to a research focus on schizophrenia, little is known about incidence among persons with bipolar disorder and other serious mental illness. While early studies suggested protective effects of schizophrenia on cancer (5), recent research shows differences in risk based on cancer site, with heightened risk for breast and lung cancer in serious mental illness but uncertainty regarding other sites, such as colon (6,7). In addition, little is known about whether racial differences in cancer in serious mental illness mirror US the US trend of higher incidence among African Americans versus whites (8). The objectives of our study were to determine the incidence of cancer in a large, community-based cohort of adults with schizophrenia and bipolar disorder, and to examine incidence by diagnosis, race, and cancer site.

## Methods

We conducted a retrospective cohort study of Maryland Medicaid adult beneficiaries with serious mental illness. The cohort included adults aged 21 to 62 years between July 1, 1992 and July 1, 1993. Included beneficiaries had two years of continuous Medicaid enrollment between July 1, 1992 and June 30, 1994. Eligible beneficiaries had a diagnosis of schizophrenia or were disabled (received Supplemental Security Income) with a diagnosis of bipolar disorder. Participants were residents of metropolitan Baltimore or the rural Eastern Shore region. The Institutional Review Boards of the Johns Hopkins School of Medicine and the Maryland Department of Health and Mental Hygiene approved the study and waived informed consent.

Medicaid administrative claims data files provided information on age, sex, race and diagnoses, which were established at cohort initiation. We defined incident cancer cases as two or more inpatient or outpatient visits with a diagnosis of cancer within one fiscal year (9). Diagnoses were identified using ICD-9 codes 140-208, 238.6, 162.2-162.5, 162.8-162.9, 174, 153, 159, 154.0-154.1, and 185. The cohort was followed through 2004. Incident cancer cases could occur between 1996 and 2004 (9).

Incidence rates were age-standardized using weights from the US 2000 population to make results comparable to estimates from the Surveillance Epidemiology and End Results (SEER) Program. The incidence rate is reported as events per 100,000 person-years. The SEER Program collects data from population-based registries. The SEER 2002-2006 data – the period closest to the study period for which SEER calculated incidence – cover 28% of the US population, yielding the most comprehensive national incidence estimates available (8).

Standardized incidence ratios (SIRs) were calculated to compare cancer incidence among the Maryland Medicaid cohort to the SEER population for breast, lung, colorectal, prostate, and total cancers. Total cancers included all cancer except non-melanoma skin cancer. We estimated all SIRs by race, sex, and diagnosis. We used Cox proportional hazards models, controlling for age and sex, to estimate the relative hazard of developing cancer among participants with schizophrenia or bipolar disorder for African Americans versus whites.

## Results

The cohort included 2,315 beneficiaries with schizophrenia and 1,002 beneficiaries with bipolar disorder. The mean ages were 41.5(10.2) and 42.9(10.7) years for adults with schizophrenia or bipolar disorder, respectively. One thousand two hundred and four (52%) beneficiaries with schizophrenia and 271 (27%) beneficiaries with bipolar disorder were

male. Among persons with schizophrenia, 1296 (56%) were African-American and 995 (43%) were white, compared to 451 (45%) and 541 (54%) among cohort members with bipolar disorder.

The SIRs comparing total cancer incidence among the study cohort with serious mental illness to the SEER population were 2.6 (95% CI: 2.2-3.0) and 2.6 (95% CI: 2.0-3.2) for persons with schizophrenia or bipolar disorder. Elevated risk of cancer compared to the SEER data was observed in all subgroups with the exception of males with bipolar disorder where the SIR estimate was 1.5 but the 95%CI was not significant (0.8-2.6). Lung cancer incidence among participants with schizophrenia or bipolar disorder was more than four times higher than the SEER population. Incidence of colorectal cancer was similarly elevated, with SIRs of 3.5 (95% CI: 2.1-5.5) for persons with schizophrenia and 4.0 (95% CI: 2.0-7.2) for persons with bipolar disorder. Female participants had heightened risk of breast cancer, with SIRs of 2.9 (95% CI: 2.1-3.9) and 1.9 (95% CI: 1.1-3.0) among women with schizophrenia or bipolar disorder, respectively. For prostate cancer, males with schizophrenia had an SIR of 1.9 compared to the US population, but this did not reach statistical significance. Males with bipolar disorder did not show increased risk for prostate cancer.

Controlling for age and sex, the hazard ratio comparing risk of all cancer among African Americans with schizophrenia versus whites with schizophrenia was 0.95 (95% CI: 0.7-1.3). The adjusted hazard ratio for cancer for cohort members with bipolar disorder was 0.88 (95% CI: 0.6-1.3).

## Discussion

This retrospective cohort study used Maryland Medicaid administrative data to examine cancer incidence by diagnosis, race, and cancer site among adults with schizophrenia or bipolar disorder. Cohort members with each diagnosis experienced higher total cancer incidence in addition to heightened risk of lung, breast, and colorectal cancer. Unlike in the overall US population, there were no racial differences in cancer risk.

The more than double risk of cancer observed among the study cohort is similar in magnitude to the result of a 2006 study using probabilistic methods by Pandiani et al (10). Our study used a longitudinal design and examined incidence by diagnosis and race and, unlike a previous study that compared cancer incidence in participants with schizophrenia and bipolar disorder and found elevated risk of cancer among the group with schizophrenia only (6), our results show heightened risk for cancer among persons with both diagnoses.

Increased risk for site-specific cancers suggests that risk factors disproportionately prevalent in the serious mental illness population increase risk for certain types of cancer. High rates of smoking among the population with serious mental illness likely contribute to lung cancer incidence, and research suggests a possible but inconclusive elevated risk of breast cancer due to low parity and increased prolactin levels caused by use of particular psychotropic medications (5). The risk factors contributing to high risk of colon cancer are less well understood, but may be related to smoking, sedentary lifestyle or diet high in fat and low in fruits and vegetables (11).

This study was limited by use of Medicaid administrative data. To address concerns about reliability and validity of diagnoses, we defined cases using methods validated by a 2003 study that demonstrated the ability of Ohio Medicaid claims data to identify incident breast cancer cases (9). We are unable to determine the stage of cancer at diagnosis and the Medicaid sample does not include all persons with schizophrenia or bipolar disorder in the state; some persons with serious mental illness may have private insurance or be covered by

social security disability insurance rather than SSI, and this group is likely of higher socioeconomic status than the study population. However, a 2010 study shows that 87% of persons with schizophrenia receive government health insurance like Medicaid, suggesting that our population is likely representative of much of the population of interest (12). In addition, the Medicaid sample by definition covers an insured population, while the SEER data is population-based and includes persons without insurance.

## Conclusions

Adults with both schizophrenia and bipolar disorder have heightened risk for total cancers and lung, colorectal and breast cancers specifically, with no differences between African Americans and whites. Better understanding of how behavioral and pharmacological factors increase cancer risk in persons with serious mental illness, and more information on the extent to which the population receives appropriate cancer screening and treatment will be important to improve health in this vulnerable group. With primary care providers, clinicians and mental health system administrators should promote appropriate cancer screening and work to reduce modifiable risk factors, such as smoking, among persons with serious mental illness.

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	Number of events	Person-years at risk	Incidence rate *	SIR (95% CI)
<b>Maryland Medicaid (1996–2004)</b>				
Schizophrenia (N=2,315)				
All sites	155	19855	468.8	2.6(2.2–3.0)
Lung	28	20675	82.1	4.7(3.1–6.8)
Colorectal	19	20709	55.0	3.5(2.1–5.5)
Female breast	42	9843	209.8	2.9(2.1–3.9)
Prostate	10	10688	92.4	1.9(0.9–3.4)
Bipolar (N=1,002)				
All sites	75	8405	477.9	2.6(2.0–3.2)
Lung	13	8935	74.8	4.1(2.2–7.2)
Colorectal	11	8923	62.7	4.0(2.0–7.2)
Female breast	16	5547	139.5	1.9(1.1–3.0)
Prostate	1	3321	17.2	0.4(0.0–2.5)
<b>SEER (2002–2006)</b>				
All sites	--	--	462.9	--
Lung	--	--	63.1	--
Colorectal	--	--	49.1	--
Female breast	--	--	123.8	--
Prostate	--	--	159.3	--
<b>Male</b>				
<b>Maryland Medicaid (1996–2004)</b>				
Schizophrenia (N=1,196)				
All sites	59	10401	437.2	2.6(2.0–3.4)
Lung	12	10691	138.0	5.0(2.6–8.8)
Colorectal	9	10722	68.9	3.8(1.7–7.1)
Prostate	10	10688	92.4	1.9(0.9–3.4)
Bipolar (N=369)				
All sites	13	3237	244.5	1.5(0.8–2.6)
Lung	3	3313	51.0	3.2(0.6–9.3)
Colorectal	4	3289	91.9	4.7(1.3–12.0)
Prostate	1	3321.0	17.2	0.4(0.0–2.5)
<b>SEER (2002–2006)</b>				
All sites	--	--	541.8	--
Lung	--	--	77.7	--
Colorectal	--	--	57.3	--
Prostate	--	--	159.3	--
<b>Female</b>				
<b>Maryland Medicaid (1996–2004)</b>				
Schizophrenia (N=1,119)				
All sites	96	9454	513.1	2.6(2.1–3.2)
Lung	16	9984.0	92.6	4.8(2.7–7.8)

	Number of events	Person-years at risk	Incidence rate*	SIR (95% CI)
Colorectal	10	9987	47.0	3.5(1.7–6.5)
Female breast	42	9843	209.8	2.9(2.1–3.9)
<b>Bipolar (N=633)</b>				
All sites	62	5168	603.3	3.0(2.3–3.9)
Lung	10	5622	81.9	4.9(2.4–9.1)
Colorectal	7	5634	55.8	4.1(1.7–8.5)
Female breast	16	5547	139.5	1.9(1.1–3.0)
<b>SEER (2002–2006)</b>				
All sites	--	--	408.5	--
Lung	--	--	52.5	--
Colorectal	--	--	42.8	--
Female breast	--	--	123.8	--
<b>White</b>				
<b>Maryland Medicaid (1996–2004)</b>				
Schizophrenia (N=990)				
All sites	74	8428	506.0	2.7(2.1–3.4)
Lung	13	8829	82.1	4.7(2.5–8.1)
Colorectal	6	8861	39.9	2.5(0.9–5.4)
Female breast	21	4409	216	2.9(1.8–4.4)
Prostate	2	4333	53.8	1.0(0.1–3.6)
<b>Bipolar (N=542)</b>				
All sites	44	4486	525.0	2.7(2.0–3.5)
Lung	5	4839	51.8	2.8(0.9–6.5)
Colorectal	7	4798	69.8	4.8(1.9–9.8)
Female breast	11	3123	176.6	2.2(1.1–4.0)
Prostate	1	1647	28.7	0.8(0.0–4.3)
<b>SEER (2002–2006)</b>				
All sites	--	--	470.6	--
Lung	--	--	64.4	--
Colorectal	--	--	48.6	--
Female breast	--	--	127.8	--
Prostate	--	--	153	--
<b>African-American</b>				
<b>Maryland Medicaid (1996–2004)</b>				
Schizophrenia (N=1,294)				
All sites	79	11156	442.7	2.2(1.7–2.7)
Lung	15	11567	83.0	3.3(1.8–5.4)
Colorectal	13	11569	69.2	3.4(1.8–5.8)
Female breast	20	5270	199.4	2.7(1.7–4.2)
Prostate	8	6247	115.2	1.4(0.6–2.7)
<b>Bipolar (N=447)</b>				
All sites	30	3807	428.2	2.1(1.4–3.0)

	Number of events	Person-years at risk	Incidence rate <sup>*</sup>	SIR (95% CI)
Lung	8	3979	99.2	4.3(1.8–8.4)
Colorectal	4	4008	61.5	2.6(0.7–6.6)
Female breast	5	2343	119.6	1.4(0.5–3.3)
Prostate	0	1638	0.0	--
<b>SEER (2002–2006)</b>				
All sites	--	--	493.6	--
Lung	--	--	74.7	--
Colorectal	--	--	59.9	--
Female breast	--	--	117.7	--
Prostate	--	--	239.8	--

\* Incidence rate is age-standardized and reported as events per 100,000 person-years.