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Colorectal Cancer Incidence and Screening in U.S. Medicaid Patients with and without HIV Infection

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Abstract

Non-AIDS defining malignancies, particularly colorectal cancer (CRC), may be more prevalent among persons living with HIV (PLWH). Further, PLWH may be less likely to receive CRC screening (CRCS). We studied the epidemiology of CRC and CRCS patterns in patients with and without HIV in a large US Medicaid population. We performed a matched cohort study examining CRC incidence in 2006 and CRCS between 1999 and 2007. Study participants were continuously enrolled in the Medicaid programs of California, Florida, New York, Ohio, and Pennsylvania. All HIV-infected enrollees were matched to five randomly sampled HIV-uninfected enrollees on five-year age group, sex, and state. Adjusted odds ratios (AORs) for incident CRC (adjusted for comorbidity index) and the presence of CRCS (adjusted for comorbidity index and years in the

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dataset) among PLWH compared to HIV-negative enrollees were calculated. PLWH were not more likely to be diagnosed with CRC after adjusting for comorbidity index (AOR 1.29; 95% CI: 0.98-1.70). While CRCS rates were low overall, PLWH were more likely to have received CRCS in unadjusted analyses (35.8% vs. 33.7%; OR 1.10, 95% CI: 1.07-1.13). This relationship reversed after adjusting for comorbidity index and years in the dataset (AOR: 0.80, 95% CI: 0.77-0.83). In conclusion, PLWH were not more likely to be diagnosed with CRC. In adjusted analyses, PLWH were less likely to have received CRCS. We showed a low rate of CRCS overall. Work should be done to improve CRC screening rates for all patients, particularly those with HIV.

Keywords

HIV; colorectal cancer; non-AIDS defining malignancies; Medicaid; colorectal cancer screening

Introduction

As HIV-infected patients live longer in the highly-active antiretroviral therapy (ART) era, they become more susceptible to the development of chronic diseases and cancers. Since the introduction of ART in 1995, the incidence of AIDS-defining malignancies (ADM) has declined. However, there is evidence that non-ADMs are rising rapidly and disproportionately in persons living with HIV (PLWH) relative to the general population (Frisch, Biggar, Engels, Goedert, & AIDS-Cancer Match Registry Study Group, 2001; Engels et al., 2008; Patel et al., 2008; Silverberg et al., 2011).

CRC is the second leading cause of cancer death in the United States (US) among malignancies that affect both men and women (US Cancer Statistics Working Group, 2013). Studies looking at colorectal cancer (CRC) risk in PLWH have been mixed. Some studies have shown that compared to HIV-uninfected individuals, PLWH may have worse survival (Berretta et al., 2009), more advanced disease at presentation (Bini, Green, & Poles, 2009), more neoplasms (Bini et al., 2009), a diagnosis at an earlier age (Kumar et al., 2012; Wasserberg, Nunoo-Mensah, Gonzalez-Ruiz, Beart, & Kaiser, 2007), or increased rates of CRC (Patel et al., 2008). Other studies have shown that PLWH either have no difference in incidence of CRC (Silverberg et al., 2011) or a lower incidence of CRC (Frisch et al., 2001; Engels et al., 2008; Silverberg et al., 2011; Van Leeuwen et al., 2009) than those without HIV.

For those at average risk for CRC, current US guidelines for CRC screening (CRCS) recommend that patients over 50 years of age have either a fecal occult blood test (FOBT) every year, sigmoidoscopy or barium enema every 5 years with FOBT every three years, or colonoscopy every ten years (Whitlock, Lin, Liles, Beil, & Fu, 2008). Screening is underutilized: in 2010, only 64.5% of respondents aged 50-75 years nationwide reported having had one of these recommended screening measures within the allotted interval (Joseph, King, Miller, & Richardson, 2012). Guidelines for PLWH recommend following standard CRCS recommendations (Phillips & Justman, 2009), but studies suggest that PLWH may be less likely to receive CRCS (Iqbal, Browne-McDonald, & Cerulli, 2010;

Momplaisir, Long, Badolato, & Brady, 2012; Reinhold, Moon, Tenner, Poles, & Bini, 2005; Campbell & Young, 2008).

There is strong evidence that many non-ADMs are increased in patients with HIV when compared with the general population. It is still unclear whether patients with HIV are at increased risk for CRC than those without HIV. Understanding this is important to determining whether current screening recommendations should be revised for PLWH. Medicaid is the nation's principal safety-net health insurance program, financing health for 62 million low-income Americans (Centers for Medicare and Medicaid Services [CMS], 2013). Medicaid is also the single largest source of coverage for PLWH in the US, covering an estimated 200,000 to 240,000 PLWH (CMS, 2013; Bozzette et al., 1998). Relatively little is known about CRCS in Medicaid populations, although it appears to be lower than in the general population (DuBard, Schmid, Yow, Rogers, & Lawrence, 2008). Thus we sought to evaluate the epidemiology of CRC and CRCS usage in a Medicaid population of PLWH and persons without HIV, hypothesizing that PLWH are at higher risk of developing CRC, and that PLWH are less likely than those without HIV to undergo CRCS.

Methods

Data Source

The Medicaid program consists of state-run programs with joint federal and state funding for hospital, medical, and outpatient care and drug benefits for low-income and special-needs individuals (CMS, 2013). In the five states used in this study (California, Florida, New York, Ohio, and Pennsylvania), 24 million persons are actively enrolled in Medicaid, representing 38% of the U.S. Medicaid population (Kaiser Family Foundation [KFF], 2011). Medicaid claims report demographic information, inpatient and outpatient medical diagnoses (recorded by using International Classification of Diseases, Ninth Revision, diagnosis codes), and medications dispensed (CMS, 2013). Since 17% of Medicaid beneficiaries are co-enrolled in Medicare, we obtained Medicare data on dually-eligible persons (CMS, 2013). The University of Pennsylvania Institutional Review Board reviewed and approved the protocol, and a data use agreement was obtained from the Centers for Medicare and Medicaid Services.

Eligibility Criteria

We performed a retrospective matched cohort study of California, Florida, New York, Ohio, and Pennsylvania state Medicaid programs. Medicare data was merged into the analytic file for those who were identified as dually-eligible for Medicare and Medicaid. To verify enrollment in Medicaid, eligible participants had to have at least one claim in both 2004 and 2005. Those with a CRC diagnosis prior to 2006 were excluded from the dataset.

From the base analytic file we created two sub-files to analyze CRC incidence and CRCS. For both sub-files, a stratified random sample of HIV-uninfected patients was matched to a stratified random sample of PLWH in a one-to-five ratio on gender, five-year age group, and state. For the sub-file to analyze CRC incidence, patients were eligible if they were at least

40 years of age on January 1, 2006. For the sub-file to analyze CRCS, patients were eligible if they were between the ages of 50 and 75 on January 1, 2006.

Variable Definitions

Patients were considered to have HIV if they had an International Classification of Disease (ICD-9) code for HIV or AIDS and a prescription for an antiretroviral medication prior to January 1, 2006. Fultz et al. (2006) showed that this algorithm had a sensitivity of 90.4% and a specificity of 99.9% for HIV diagnosis. Age was calculated as the age of patients on January 1, 2006. Age within each five-year age group (e.g., 40-44, 45-49, 50-54, 55-59, etc.) was coded as a continuous variable. Race codes were abstracted from Medicaid and were coded as white race, black race, Hispanic ethnicity (regardless of race), or other race/ethnicity, with white as the referent race/ethnicity group. Numbers of years in the dataset was calculated from the first claim to the final claim. Numbers of diagnoses coded was calculated and dichotomized as greater than or less than 120 codes. Comorbidity scores were based on Chronic Illness Disability Payment System (CDPS) scores and ranged from 1 to 33. CDPS scores are based on weighted ICD-9 codes and have been validated in Medicaid datasets (higher scores are associated with higher health services utilization) (University of California, San Diego [UCSD], 2012). Comorbidity scores were calculated based on the participant's first six months in the dataset, with codes reflective of HIV or AIDS removed.

Patients were considered to have incident CRC if they had a new Common Procedural Terminology (CPT) code for CRC in 2006 and none prior to 2006. We used an algorithm validated by Setoguchi et al. (2007) using Medicare data to define incident CRC cases associated with 80.36% sensitivity and 99.51% specificity. Using this algorithm, patients were considered to have incident CRC if they had a new Common Procedural Terminology (CPT) code or an International Classification of Diseases classification system (ICD-9 code) for CRC in 2006 and none prior to 2006.

Patients were considered to have received CRCS if they had a CPT code for a sigmoidoscopy, colonoscopy, or barium enema between January 1, 1999 and December 31, 2007. Type of screening as well as codes for the location of CRCS (inpatient or outpatient) were also determined and reported. Validation studies using Medicare data shows that claims for CRCS have a sensitivity of 93% to 97% and a specificity of 91% to 95% (Schenck et al., 2007). We assumed that the same would be true for Medicaid claims. However, the indication for testing (i.e. screening vs. diagnosis) has been unreliable in Medicare data (Schenck et al., 2007).

As an additional analysis, we investigated whether access to primary care providers (PCPs) was associated with CRCS. We used as our measure of access, the number of PCPs per 100,000 persons in the patients' home zip code. This count was determined from the Dartmouth Atlas Project (Goodman et al., 2003) and divided into quartiles.

Data Analysis

For CRC, we calculated the incidence of CRC as the proportion of new CRC diagnoses per 100,000 person-years. ORs with 95% CIs compare the CRC incidence in PLWH to HIV-uninfected individuals. Logistic regression was used to calculate adjusted ORs (AOR).

Covariates considered included race, comorbidity index, time in the dataset, and an interaction term between race/ethnicity and HIV. Covariates were retained in the model if they caused a change in the estimate by at least 10%.

For CRCS, we calculated the prevalence of CRCS in both HIV-infected and uninfected individuals, as well as the odds of receiving CRCS in PLWH as compared to HIV uninfected individuals. Covariates considered in the logistic regression model included race, comorbidity index, PCP density, time in the dataset, and an interaction term between race/ethnicity and HIV. Again, covariates were retained in the model if they were associated with a change in the point estimate by at least 10%. Finally, location of CRCS and type of CRCS (barium enema, colonoscopy, or sigmoidoscopy) were compared between PLWH and HIV-uninfected patients.

Results

Analysis of CRC Incidence

For the CRC incidence portion of the study, 55,439 PLWH were matched to 277,195 HIV-negative patients (Table 1) [insert Table 1 near here]. PLWH were more likely to be black (42.4% vs. 19.5%) or Hispanic (24.1% vs. 22.6%). PLWH had more years in the dataset (7.98 years vs. 7.22 years), had a higher comorbidity index (7.45 vs. 3.44), and lived in places with more PCPs per 100,000 residents (80.67 vs. 77.11).

There were 94 PLWH (169.6 per 100,000 person-years) and 271 patients without HIV (97.8 per 100,000 person-years) diagnosed with CRC. PLWH who were diagnosed with CRC were diagnosed at a younger age than those without HIV who were diagnosed with CRC (53.51 vs. 55.68 years, p=0.046). Those with CRC and HIV were more likely to be of black race than those with CRC who did not have HIV (37.2% vs. 21.0%, p=0.002), while those with CRC and HIV were less likely to be of “other” race/ethnicity than those with CRC without HIV (5.3% vs. 17.0%, p=0.002). Of those diagnosed with CRC, PLWH were more likely to be in the dataset longer (8.02 vs. 7.00 years, p<0.001) and to have a higher comorbidity index (8.97 versus 4.72, p<0.001). In unadjusted analyses, PLWH were more likely to have been diagnosed with CRC in 2006 (OR: 1.73, 95% CI: 1.37-2.19, p<0.001). Only comorbidity index was retained in the model. After adjusting for comorbidity index, there was no significant relationship between HIV status and CRC diagnosis (adjusted OR: 1.29, 95% CI: 0.98-1.70, p=0.058).

Analysis of CRCS

In our analysis of CRCS, 22,928 PLWH were matched to 114,640 HIV-negative patients. PLWH were more likely to be black than those who were HIV-negative (44.1% vs. 18.5%) (Table 2) [insert Table 2 near here]. Half of the patients in each dataset were from New York State (50.7%). PLWH were in the dataset longer and had a higher comorbidity index.

Of the CRCS dataset, 35.8% of PLWH were screened compared to 33.7% of those who were uninfected. Compared to those who were uninfected, the unadjusted odds of screening in PLWH was 1.10 (95% CI: 1.07-1.13). However, after adjusting for comorbidity index and years in the dataset, PLWH had a 25% lower odds of being screened for CRC (AOR: 0.80,

95% CI: 0.77-0.83, p<0.001). Most patients were screened with colonoscopy (Table 3), although this was slightly more common in those without HIV (86.0% vs. 86.7%) [insert Table 3 near here]. PLWH were more likely to have had a sigmoidoscopy (9.7% vs. 7.2%).

Discussion

In this analysis of a large Medicaid dataset, we found that after adjusting for comorbidity, PLWH had similar rates of CRC as uninfected individuals. While PLWH were less likely to receive CRCS, the difference was small.

Studies on the relationship between CRC and HIV have been mixed. Many studies have suggested that PLWH were more likely to be diagnosed with CRC, often at an earlier age or with a more aggressive malignancy (Patel et al., 2008; Berretta et al., 2009; Bini et al., 2009; Kumar et al., 2012; Wasserberg et al., 2007). However, many of these studies were single-center (Berretta et al., 2009; Wasserberg et al., 2007), and most did not adjust appropriately for age. As described in Shiels, Pfeiffer, and Engels (2010), the population of PLWH is younger than the overall population of the US. When this group adjusted for the age difference in those with HIV, they saw no difference in CRC incidence (Shiels et al., 2010). Our study showed that when matched on age, gender, and state and after adjusting for comorbidity index, there was no significant difference between CRC incidence in HIV-infected and uninfected populations. This is in agreement with the prior studies that did not show an increase in CRC incidence in PLWH (Frisch et al., 2001; Engels et al., 2008; Patel et al., 2008; Silverberg et al., 2011; van Leeuwen et al., 2009).

Overall PLWH were more likely to have received CRCS, but once adjusted for comorbidity index and years in the dataset, PLWH were less likely to have received CRCS. Several small studies have suggested that PLWH were less likely to have received CRCS (Iqbal et al., 2010; Momplaisir et al., 2012; Reinhold et al., 2005). However, Chang, Asch, and Werner's (2010) study of cancer screenings in obesity suggested that the presence of comorbidities may increase the likelihood of receipt of preventative screenings and vaccinations, with the possible exception of CRCS. In other words, in Chang et al. (2010), those with obesity may have had more clinical visits, and thus more opportunities to discuss preventative screenings. Our study supports this—overall, PLWH were more likely to receive CRCS, but this relationship no longer existed after adjusting for comorbidities and time in the dataset.

However, CRCS in this dataset of Medicaid patients was low overall. In our study, 35.8% of PLWH received CRCS, and 33.7% of those without HIV received CRCS. In the US overall, 64.5% of those over the age of 50 have received CRCS (Joseph et al., 2012). This is actually higher than the 28.2% CRCS prevalence among a North Carolina Medicaid population (DuBard et al., 2008). Patients on Medicaid are primarily of low socioeconomic status and with preexisting medical conditions (CMS, 2013). Some of these preexisting disabilities may include psychiatric conditions which may make them less likely to agree to CRCS (van Hout, de Wit, Rutten, & Peeters, 2011). Patients on Medicaid may have a lower health literacy than those with employer-based insurance (Kuther, Greenberg, Jin, & Paulsen, 2006), so may be less likely to agree to CRCS. Furthermore, patients who are low-income may be more likely to be workers in hourly-wage jobs. These jobs may make it more

difficult for patients to take time off work for a procedure such as a colonoscopy or sigmoidoscopy including recovery from sedation. Finally, providers—including gastroenterologists performing CRCS, as well as PCPs referring patients for CRCS--may not accept Medicaid insurance. Thus, Medicaid patients may struggle to access CRCS.

Improving the rates of CRCS in Medicaid populations is particularly important in the setting of the Affordable Care Act (ACA). The ACA will lead to an expansion in Medicaid enrollment. However if patients using Medicaid already have trouble accessing providers of CRCS, policy-makers should ensure that PCPs and providers of CRCS can accept more Medicaid patients. Ideas to improve healthcare quality overall, such as the Patient Centered Medical Home and Value-Based Purchasing, may provide opportunities for providers to improve CRCS rates among Medicaid patients.

Our study was subject to several limitations. It is possible that the low rate of CRCS in our dataset was due to the fact that half of the patients in the CRCS dataset were between the ages of 50 and 55 years. Perhaps with a few extra years, more patients would have received CRCS. However, other studies of CRCS have looked at Americans starting at 50 years of age (DuBard et al., 2008). Despite this, our CRCS rates were still low. Studies of Medicaid populations have also demonstrated low CRCS rates (Joseph et al., 2012; DuBard et al., 2008). This may be due to the fact that we did not include claims for fecal occult blood testing (FOBT) since FOBT coding in Medicaid has not been validated nor well documented. However, we felt comfortable with this decision since most Americans receive CRCS through colonoscopy, sigmoidoscopy, or barium enema (Subramanian, Klosterman, Amonkar, & Hunt, 2004). In using a Medicaid dataset, our patients were likely of a lower SES and possibly sicker than the overall population, so our results may not apply to PLWH, or persons in the US, as a whole. With a longer follow-up period, we would have identified more CRC cases—perhaps enough for a more precise estimate of the relationship between HIV and CRC. However, our dataset included a large number of patients in five states, which should have given us a precise estimate. Finally, we were unable to investigate the reasons for CRCS, as documentation of reasons for screening were inconsistent.

Our study has several strengths. It is the first to examine the relationship between HIV and CRC and CRCS in a Medicaid dataset, a major provider of HIV care in the United States. We used a well-validated algorithm to identify colonoscopy and sigmoidoscopy, and think that it is unlikely that a patient would have received these procedures without submitting a claim. Finally, our dataset was large enough that we should have been able to see a relationship between HIV and CRC, or HIV and CRCS, where they existed.

In conclusion, we have demonstrated that when adjusting for comorbidities, and matched on age, gender, and state, there is no statistically significant difference in CRC incidence in those with and without HIV in a large Medicaid dataset. We also demonstrated that when adjusted for comorbidity index and time in the dataset, those with HIV are less likely to receive CRCS. However, CRCS rates were very low overall, indicating that efforts are needed to improve CRCS rates in all Medicaid patients, including PLWH.

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Table 1

Characteristics of those in the colorectal cancer incidence analytic sub-file.*

	HIV+ patients (N=55,439)	HIV- patients (N=277,195)	p-value
Age, Mean, SD	49.89, 7.28	49.98, 7.41	0.010
Female Gender, n (%)	18,068 (32.6%)	90,340 (32.6%)	1.0
Race/Ethnicity, n (%)			
White	15,001 (27.1%)	118,357 (42.7%)	<0.001
Black	23,419 (42.2%)	54,100 (19.5%)	<0.001
Hispanic	13,365 (24.1%)	62,657 (22.6%)	<0.001
Other	3,654 (6.6%)	42,081 (15.2%)	<0.001
State of Medicaid Enrollment, n (%)			
California	12,797 (23.1%)	63,985 (23.1%)	1.0
Florida	11,945 (21.5%)	59,725 (21.5%)	1.0
New York	27,326 (49.3%)	136,630 (49.3%)	1.0
Ohio	1,957 (3.5%)	9,785 (3.5%)	1.0
Pennsylvania	1,414 (2.6%)	7,070 (2.6%)	1.0
Years in the Dataset, Mean, SD	7.98, 1.62	7.22, 2.02	<0.001
Comorbidity Index, Mean, SD	7.45, 3.33	3.44, 3.00	<0.001
Primary Care Provider Density per 100,000, Mean, SD	80.67, 14.84	77.11, 13.53	<0.001
Colorectal Cancer Diagnosis	94 (0.2%)	271 (0.1%)	<0.001

* Patients were matched on state, five-year age group, and gender. Differences were considered statistically significant at $\alpha<0.05$. SD=Standard Deviation; HIV=Human Immunodeficiency Virus

Table 2

Characteristics of those in the colorectal cancer screening analytic sub-file.*

	HIV+ patients (N=22,928)	HIV- patients (N=114,640)	p-value
Age, Mean, SD	56.45, 5.42	56.66, 5.51	<0.001
Female Gender, n (%)	7,004 (30.5%)	35,020 (30.5%)	1.0
Race/Ethnicity, n (%)			
White	5,783 (25.2%)	48,254 (42.1%)	<0.001
Black	10,103 (44.1%)	2,130 (18.5%)	<0.001
Hispanic	5,314 (23.2%)	25,704 (22.4%)	<0.001
Other	1,728 (7.5%)	19,452 (17.0%)	<0.001
State: California	5,050 (22.0%)	25,250 (22.0%)	1.0
Florida	5,075 (22.1%)	25,375 (22.1%)	1.0
New York	11,624 (50.7%)	58,120 (50.7%)	1.0
Ohio	658 (2.9%)	3,290 (2.9%)	1.0
Pennsylvania	521 (2.3%)	2,605 (2.3%)	1.0
Years in the Dataset, Mean, SD	8.07, 1.56	7.25, 2.01	<0.001
Comorbidity Index, Mean, SD	7.92, 3.48	4.03, 3.22	<0.001
Primary Care Provider Density per 100,000, Mean, SD	81.17, 14.92	77.64, 13.68	<0.001
Colorectal Cancer Screening	8,213 (35.8%)	38,607 (33.7%)	<0.001

*Patients were matched on state, five-year age group, and gender. Differences were considered statistically significant at $\alpha<0.05$.

SD=Standard Deviation; HIV: Human Immunodeficiency Virus

Table 3

Type of and reason for colorectal cancer screening, among patients with and without HIV who received colorectal cancer screening.*

	HIV+ patients (N=8,213)	HIV- patients (N=38,607)	p-value
Screening Location, n (%)			
Inpatient	1091 (13.3%)	3310 (8.6%)	<0.001
Outpatient	7209 (87.8%)	35737 (92.6%)	<0.001
Inpatient and Outpatient	87 (1.1%)	440 (1.1%)	0.531
Procedure, n (%)			
Colonoscopy	6015 (86.0%)	29927 (86.7%)	<0.001
Sigmoidoscopy	680 (9.7%)	2475 (7.2%)	<0.001
Barium Enema	303 (4.3%)	2098 (6.1%)	<0.001

*Of patients included in the matched colorectal cancer screening dataset. Patients were matched on state, five-year age group, and gender. Relationships are considered statistically significant at a<0.05.

HIV=Human Immunodeficiency Virus