

Suboptimal Rates of Cervical Testing Among Women With Inflammatory Bowel Disease

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Background & Aims: Women with IBD have a high incidence of abnormal cervical cytology. However, little is known about how frequently women with IBD are tested for cervical abnormalities. We aimed to determine cervical testing rates among women with IBD, specifically those on immunosuppressant medications, and to identify risk factors associated with low incidence of screening. **Methods:** With the PharMetrics Patient-Centric Database from 1996–2005, we identified cases of IBD and matched controls via a validated algorithm. With logistic regression, we compared utilization of cervical testing with IBD case status, patients' age, use of immunosuppressive medications, Medicaid insurance status, and use of primary care services. **Results:** Only 70.4% of women with IBD (n = 9356) and 65.2% of matched controls (n = 25,849) received cervical testing (at least once every 3 years). Women with IBD who used primary care services had increased odds of cervical testing (odds ratio [OR], 1.37; 95% confidence interval [CI], 1.19–1.59). Factors associated with reduced testing included Medicaid insurance (OR, 0.28; 95% CI, 0.19–0.41), immunosuppressant medication use (OR, 0.81; 95% CI, 0.74–0.88), and increased age (P for trend < .01). Among women on immunosuppressive medications (n = 7415), 50.1% were tested during a 15-month period. Women on immunosuppressive medications who used primary care services have improved odds of cervical testing (OR, 1.28; 95% CI, 1.14–1.45), whereas those with Medicaid insurance had reduced odds (OR, 0.54; 95% CI, 0.39–0.74). **Conclusions:** Women with IBD are tested for cervical abnormalities at suboptimal rates. Quality improvement initiatives are needed to improve disease prevention services for women with IBD.

It is estimated that 11,070 women will be diagnosed with cervical cancer and 3,870 women will die of cancer of the cervix in 2008.¹ A much higher percentage of women will develop abnormal cervical pathology, a precursor to cervical cancer. The American College of Obstetrics and Gynecology (ACOG) and the American Cancer Society (ACS) recommend screening with Pap smear at least every 3 years for all women and annual screening for women greater than 30 years of age and women who are immunosuppressed.^{2,3} This is due to the

risk of human papilloma virus (HPV) infection leading to dysplasia among immunosuppressed women. Although cervical malignancy is largely preventable with proper screening, it is estimated that 50% of women who receive diagnoses of cervical cancer have never been screened.²

Women with IBD are a population that commonly use immunosuppressant medications and might thus be at higher risk for cervical abnormalities. Currently, it is unclear whether there is also an increased risk of cervical cancer in this population. Two recent studies found a higher proportion of abnormal Pap smears in women with IBD compared with matched controls.^{4,5} One of these studies found that this increased risk was associated with immunosuppression.⁴ These findings suggest that although screening for cervical dysplasia is recommended for all women, this is a particularly important component of healthcare maintenance and prevention for women with IBD.

Despite the importance of performing recommended Pap smear screening in women with IBD, a growing body of literature suggests that women with IBD⁶ and other chronic illnesses⁷ do not receive optimal screening and preventive care. If women with IBD have an increased risk of cervical abnormalities and a reduced rate of screening, this represents an area to intervene with quality improvement initiatives and potential guidelines for vaccination. Therefore, by using a large administrative database, we sought to compare the actual rate of cervical testing in women with and without IBD. We also sought to determine whether the high-risk subgroup of women with IBD who were on immunosuppressant medications were more likely to be screened. Our secondary aim was to identify factors associated with reduced Pap smear testing rates, such as age, insurance status, and use of primary care services.

Methods

Study Design and Data Source

In this cross-sectional study, we analyzed the medical, surgical, and pharmaceutical insurance claims contained in the PharMetrics Patient-Centric Database (IMS Health, Watertown, MA) for the period August 1, 1996 through June 30, 2005. This

Abbreviations used in this paper: ACOG, American College of Obstetrics and Gynecology; ACS, American Cancer Society; CI, confidence interval; HPV, human papilloma virus; Ob/Gyn, obstetrics and gynecology provider; OR, odds ratio; PCP, primary care provider; USPSTF, United States Preventive Services Task Force.

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longitudinal, patient-level database has been used in previous epidemiologic studies of IBD,⁸ and at the time of this study it included claims from 87 health plans in 33 states. Prior studies have reported PharMetrics to be representative of the national commercially insured population on a variety of demographic measures, including geographic region, age, gender, and health plan type.⁹

Patient Selection

All female patients aged 20–64 years with at least 36 months of continuous health plan enrollment were eligible for inclusion in this analysis. We chose an initial age of 20 because guidelines recommend initiation of Pap smears 3 years after the onset of sexual activity (median age of first intercourse for women is 17.4)¹⁰ or age 21. We chose 64 as the upper limit for evaluation because the United States Preventive Services Task Force (USPSTF) recommends discontinuing routine Pap smear screening at age greater than 65¹¹ and because Medicare eligibility begins at age 65. We identified cases of CD and UC by using a previously reported administrative definition.⁸ This definition included patients with at least 3 healthcare contacts, on different days, associated with an International Classification of Diseases, 9th Revision, Clinical Modification diagnosis code for CD (555.xx) or UC (556.xx), or patients with at least 1 claim for CD or UC and at least 1 pharmacy claim for any of the following medications: mesalamine, olsalazine, balsalazide, sulfasalazine, 6-mercaptopurine, azathioprine, infliximab, adalimumab, and enteral budesonide. For patients who had claims for both CD and UC, disease assignment was made according to the majority of the last 9 claims. For each case, we randomly selected up to 3 non-IBD controls, matched for age, gender, health plan, geographic region, and Medicaid exposure (patients managed by a managed Medicaid plan).

Assessment of Outcome (Cervical Testing)

We ascertained whether cervical testing was performed in each patient and control via a previously validated claims algorithm reported to have greater than 95% sensitivity and 95% specificity when compared with the medical record.¹² The algorithm heavily weighs pathology and lab codes for cervical specimen analysis as evidence of cervical testing. The dependent variable for cervical testing was coded in a binary fashion (yes/no).

Assessment of Factors Associated With Cervical Testing

We analyzed whether the following potential factors were associated with increased or decreased use of cervical testing: utilization of primary care services/provider (PCP), use of immunosuppressant medications, Medicaid insurance status (a proxy for socioeconomic status), and age. Utilization of PCP was defined as any visit to a general practitioner, internist, family practitioner, or geriatrician during the analysis window (binary yes/no). We also performed separate analyses including visits to obstetrics/gynecology providers (Ob/Gyn) in the definition of primary care utilization. Immunosuppressant medication use was defined as 2 or more filled prescriptions of at least 1 of the following medications: prednisone, azathioprine, 6-mercaptopurine, methotrexate, infliximab, or adalimumab (binary yes/no). Medicaid insurance status was speci-

fied within the dataset (binary yes/no). Age was analyzed in 10-year categories.

Additional Analyses

Analyses were then repeated for the second population of women with IBD on chronic immunosuppressant medications during a 15-month analysis window (this interval was chosen to approximate the ACOG's recommended 12-month interval for cervical testing for immunosuppressed women). Chronic use of immunosuppressant medications was defined as at least 2 claims for any of the following medications: prednisone, azathioprine, 6-mercaptopurine, methotrexate, infliximab, or adalimumab.

Statistical Analysis

Bivariate analyses with Pearson χ^2 test statistic were performed to evaluate the frequency of cervical testing during the 36-month analysis window by IBD case status and during the 15-month analysis window for IBD patients treated with chronic immunosuppression. Similar bivariate analyses were used to evaluate the association between performance of cervical testing and the following independent variables: visit to a PCP, immunosuppressant medication use, Medicaid insurance status, and age. Next, odds ratios (ORs) and 95% confidence intervals (CIs) for each of these independent variables were estimated from unconditional logistic regression models.

For all analyses, *P* values were two-sided, and a *P* value of .05 or less was considered statistically significant. All statistical analyses were performed with Stata version 9.0 (College Station, TX). Analyses were performed for the overall population of women with IBD and also stratified by UC and CD diagnosis. The study protocol was granted exemption from review by the Institutional Review Board at University of North Carolina because it involved the use of existing, de-identified data.

Results

A total of 9356 cases of women with IBD with at least 36 months of continuous health plan enrollment met our a

Table 1. Characteristics of the Population (Women With at Least 36 Months of Continuous Enrollment) by IBD Case Status^a

Characteristic	IBD (n = 9356)		No IBD (n = 25,849)	
Age	9356	44.1 (10.4)	25,849	44.2 (10.3)
Region				
East	3034	32.4%	8705	33.7%
Midwest	3292	35.2%	9473	36.7%
South	742	7.9%	1301	5.0%
West	2288	24.5%	6370	24.6%
PCP ^b	8446	90.3%	21,495	80.2%
Medicaid	107	1.1%	350	1.4%
Pap smear ^c	6583	70.4%	16,851	65.2%

^aMean (standard deviation) for continuous variables by Student *t* test, percent for categorical variables by Pearson χ^2 test statistic.

^bDefined as any visit to a PCP (internist, family practitioner, general practitioner, or geriatrician) during the 36-month period.

^cSee Appendix 1 (see supplementary material online at www.cghjournal.org) for claims algorithm for Pap smear during the 36-month study period.

Table 2. Multivariate Adjusted ORs of Factors Associated With Pap Smear Screening in U.S. Women With IBD During the 36-Month Study Period^a

	Cervical testing	
	OR	95% CI
No PCP	1.0 (referent)	
PCP	1.37	1.19–1.59
Commercial insurance	1.0 (referent)	
Medicaid insurance	0.28	0.19–0.41
No immunosuppressive medication use	1.0 (referent)	
Immunosuppressive medication use	0.81	0.74–0.88
Age (y)		
20–29	1.0 (referent)	
30–39	0.93	0.78–1.11
40–49	0.76	0.64–0.90
50–59	0.55	0.46–0.65
60–64	0.36	0.28–0.47

^aAdjusted for region of the country, Medicaid insurance, PCP visit, and age as appropriate.

priori criteria, as did 25,849 age-matched and geographically matched women without IBD. The characteristics of the population are shown in Table 1. The mean age of the IBD patients and matched controls was 44 years (standard deviation, 10). Each of the 4 major U.S. census regions was adequately represented in our patient population. More women with IBD had a primary care visit during the 36-month window ($P < .01$).

Only 70.4% of women with IBD and 65.2% of their non-IBD-matched controls received the recommended Pap smear screening during the 3-year observation period. Among those women with IBD, 71.1% who used primary care services versus 64.0% who did not use primary care services underwent appropriate testing ($P < .01$). Significantly fewer women with IBD who had Medicaid insurance, as compared with commercial insurance, were screened (43.9% versus 70.7%, respectively; $P < .01$). Slightly fewer women with IBD on immunosuppressant medications underwent cervical testing (68.3% versus 71.7%, $P < .01$). Multivariate analyses confirmed these findings; those with

a PCP had significantly increased odds of Pap smear screening, and those on Medicaid insurance, on immunosuppressive medications, and of increasing age had lower rates (Table 2). Additional analyses were performed including OB/Gyn visits in the definition of PCP visit and showed similar results of improved cervical testing with access to primary care. Women with IBD who visited a PCP or OB/Gyn were more than twice as likely to obtain a Pap smear compared with women without a PCP or OB/Gyn visit (OR, 2.28; 95% CI, 1.89–2.75).

To evaluate the possibility that women prescribed immunosuppressant medications have more severe disease and seek gastrointestinal specialty care at the expense of primary care, we analyzed the bivariate relationship between immunosuppressive use and PCP care. We found that a slightly greater percentage of women with IBD on immunosuppressive medications had primary care visits during the study period (91.8% versus 89.3%, $P < .001$).

These analyses were repeated within strata of CD and UC, and there were no differences (data not shown).

Next we analyzed whether women with IBD who might be at greater risk for cervical dysplasia as a result of immunosuppression received annual screening with Pap smears as recommended by ACOG guidelines. A total of 7415 women with IBD and 2 or more prescriptions for immunosuppressant medications were identified. The demographic characteristics of this subgroup are shown in Table 3, and in general they were similar to the overall population of women with IBD. For these high-risk women, only 50.1% were screened with a Pap smear during a 15-month window. Those who visited a PCP had a higher rate of Pap smear testing (51.0% versus 46%, $P < .01$), and those with Medicaid insurance had a significantly lower rate of Pap smear testing as compared with those with commercial insurance (37.8% versus 50.4%, respectively; $P < .01$). On multivariate analyses, those with a PCP had higher odds of Pap smear testing (OR, 1.28; 95% CI, 1.14–1.45); this was again seen when Ob/Gyn was included in the definition of PCP (OR, 2.95; 95% CI, 2.51–3.46), and those with Medicaid insurance had a lower odds of Pap smear testing (OR, 0.54; 95% CI, 0.39–0.74). Older women were also less likely to undergo cervical testing when analyzed in 10-year increments (Table 4). Analyses were repeated by using a more conservative definition of immunosuppressive medication use (azathioprine, 6-mercaptopurine, meth-

Table 3. Characteristics of the Population of Women With IBD, Overall and Stratified by UC and CD, With at Least 15 Months of Continuous Enrollment and Use of Immunosuppressant Medications^{a,b}

Characteristic	IBD (n = 7415)		CD (n = 4626)		UC (n = 2789)	
Age	7415	43.2 (11.2)	4626	42.6 (11.2)	2789	44.0 (11.1)
Region						
East	1646	22.2%	990	21.4%	656	23.5%
Midwest	2788	37.6%	1829	39.5%	959	34.4%
South	1688	22.8%	1051	22.7%	637	22.8%
West	1293	17.4%	756	16.3%	537	19.3%
PCP ^c	6068	81.8%	3786	81.8%	2282	81.8%
Medicaid	172	2.3%	133	2.9%	39	1.4%
Pap smear ^d	3717	50.1%	2263	48.9%	1454	52.1%

^aDefined as at least 2 prescriptions filled for immunosuppressant medication during this time period.

^bMean (standard deviation) for continuous variables, percent for categorical variables.

^cDefined as any visit to a PCP (internist, family practitioner, general practitioner, or geriatrician) during the 15-month period.

^dSee Appendix 1 (see supplementary material online at www.cghjournal.org) for claims algorithm for Pap smear during the 15-month period of continuous enrollment.

Table 4. Multivariate Adjusted ORs of Factors Associated With Pap Smear Screening in U.S. Women With IBD on Immunosuppressant Medications During a 15-Month Study Period^a

Cervical testing		
	OR	95% CI
No PCP	1.0 (referent)	
PCP	1.28	1.14–1.45
Commercial insurance	1.0 (referent)	
Medicaid insurance	0.54	0.39–0.74
Age (y)		
20–29	1.0 (referent)	
30–39	0.78	0.67–0.91
40–49	0.67	0.58–0.78
50–59	0.56	0.48–0.65
60–64	0.40	0.32–0.50

^aAdjusted for region of the country, Medicaid insurance, PCP visit, and age as appropriate.

otrexate, infliximab, or adalimumab but not corticosteroids). Similar to the initial analysis, women with a PCP visit had increased odds of cervical testing (adjusted OR, 1.39; 95% CI, 1.20–1.61), and women with Medicaid insurance had reduced odds of cervical testing (adjusted OR, 0.72; 95% CI, 0.46–1.12).

Discussion

In this large cross-sectional study we found that only approximately 2/3 of women with IBD received screening for cervical dysplasia and/or cancer as recommended by USPSTF, ACS, and ACOG guidelines. We also found that those women without utilization of primary care services, those who were insured by a Medicaid plan, and those at an older age were the least likely to receive this important preventive service. This suboptimal preventive care is particularly alarming, given the abundant evidence that Pap smear screening can reduce the incidence of and mortality from cervical cancer.¹¹ Indeed, although this malignancy is largely preventable with proper screening, it is estimated that 50% of women who receive diagnoses of cervical cancer have never been screened.²

These results are both timely and significant because 2 recent studies have shown an increased risk of abnormal Pap smears among women with IBD. Bhatia et al⁵ found a higher prevalence of abnormal Pap smears among women with IBD as compared with age-matched controls (18% versus 5%, respectively). Similarly, Kane et al⁴ also demonstrated an increased risk of abnormal Pap smears among women with IBD at a tertiary care referral center as compared with non-IBD controls. In this small study, women with IBD who used immunosuppressant medications had an even greater risk of having an abnormal Pap smear. With evidence of increased abnormal cervical pathology among women with IBD, it is essential to (1) determine whether U.S. women with IBD are receiving appropriate screening and (2) to identify the factors associated with reduced adherence to cervical screening recommendations.

We examined utilization patterns of cervical testing in a large, geographically diverse, population-based sample of women with IBD. A separate study of IBD patients followed at 2 Midwestern academic medical centers found that approxi-

mately 90% of patients received a Pap smear every 3 years.⁶ The lower rate of cervical screening observed here (70.4%) is more likely to reflect the care delivered to women in the broader U.S. community. Indeed, our results mirror those observed in other chronic disease processes in which immunosuppression is used, such as rheumatoid arthritis. Kremers et al⁷ evaluated utilization of preventive services among women with rheumatoid arthritis from 1987–1995 via medical record review of inpatient and outpatient records and found that only 77% complied with recommended cervical testing every 3 years.

Understanding factors related to utilization of preventive services is paramount in improving screening rates. Our finding that women who visited a PCP were more likely to receive a screening Pap smear suggests that women with IBD ought to be co-managed by a PCP along with a gastroenterologist. Nevertheless, the suboptimal cervical screening even among IBD patients who visited a PCP indicates that “missed opportunities” still exist. We also found that Medicaid insurance (as a proxy for poor socioeconomic status) was associated with poor cervical screening. Although there were small numbers of Medicaid patients within our dataset, this is an important, albeit exploratory, observation. To our knowledge, socioeconomic disparities in the screening of patients with IBD have not been previously described; however, similar social disparities in cancer screening have been reported in non-IBD populations¹³ and highlight the fact that our health system must strive for more equitable care, even among IBD patients.

The fact that we found immunosuppressive medication use to be inversely associated with cervical screening is quite concerning. If the prior studies from Kane et al⁴ and other studies from the rheumatologic literature⁷ are correct, then it appears that the women at highest risk for cervical pathology are the ones who, paradoxically, are the least likely to be screened. This high-risk yet underscreened population should be a high priority for quality improvement initiatives.

The strengths of this study include both the size and diversity of the study population. By drawing from a large number of health plans of varying size, type, and location, we believe that the results presented here are broadly generalized to the commercially insured population of the United States. Another strength of this study was the ability to use pharmacy claims to delineate use of immunosuppressive medications.

An inherent limitation to using administrative data for epidemiologic studies is the lack of clinical detail, resulting in the possibility of misclassification of our included patients. We used a stringent case definition that required either multiple IBD-related health contacts or IBD-specific pharmaceutical claims to establish a diagnosis of CD or UC. Similar administrative definitions have been previously reported by our group⁸ and others.^{14,15} Similarly, we were unable to detect Pap smears that were performed and not billed, which would result in an underestimation of the actual cervical testing in this population. However, the algorithm used to identify Pap smear utilization has been previously validated against chart review with very high sensitivity and specificity,¹² and thus we believe that we had near complete capture of the Pap smears that were performed. Because of the lack of clinical data, we were unable to assess HPV status and smoking, which are known risk factors for cervical cancer. To the extent that these are associated with the performance of Pap smears, they might represent unmeasured confounders.

Another limitation to this study is that although our data source is broadly generalizable to the commercially insured population of the United States, several populations were notably excluded from this analysis, such as the uninsured and the elderly. The uninsured might receive Pap smears through charity care, and these would not be captured in our database. However, we expect that the uninsured population may be less likely to receive preventive services such as Pap smears, and thus, the overall cervical screening provided to IBD patients in the U.S. might be even worse than that reported here. We also did not have data on patients older than the age of 65; however, given that the USPSTF only recommends cervical screening for those younger than 65 years of age, this does not represent a significant limitation.

Part of the effect of reduced cervical screening with advancing age that we observed in our study might have been related to increased rates of hysterectomy with advancing age. Approximately 23.3% of women older than 18 years of age in the United States have had a hysterectomy.¹⁶ However, the number of these procedures performed during the past decade has been decreasing. The prevalence reaches approximately 18% during the reproductive years and increases to about 48% after this (peaking at approximately age 75).¹⁶ We were unable to account for prior hysterectomy in our analysis, owing to the fact that we only had claims for a 3-year time period. Instead, we repeated our analyses exclusively in women <44 years of age (hysterectomy rate peaks between ages 45–64), and the main findings did not change (data not shown).

In summary, this study provides convincing evidence that women with IBD do not receive recommended screening for cervical dysplasia/cancer. We also found that women who are on immunosuppressive medications, those who are older, insured by Medicaid, and who do not use primary care services are the least likely to receive this important preventive service. Given recent data that women with IBD might be at increased risk for abnormal Pap smears,⁴ quality improvement initiatives are needed to improve screening rates, particularly in these vulnerable populations.

Supplementary Data

Note: to access the supplementary materials accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org.

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Conflicts of interest

The authors disclose no conflicts.

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