

**Title:** Determinants of Cervical Cancer Screening Patterns Among Women with Systemic Lupus Erythematosus

**Running title:** Cervical cancer screening in women with SLE

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## ABSTRACT

**Objective:** Women with systemic lupus erythematosus (SLE) are vulnerable to cervical dysplasia due to the persistence of human papillomavirus (HPV) infection. The objective of this cross-sectional retrospective study was to investigate the prevalence of cervical cancer screening per the American Society for Colposcopy and Cervical Pathology (ASCCP) SLE-specific cervical cancer screening guidelines. We also aimed to identify SLE-specific determinants associated with ASCCP adherence.

**Methods:** Women aged 21-64 years enrolled in our institutional SLE registry were included in the study. The medical record was manually reviewed to determine whether the patient was up to date on screening and which organizational guideline was utilized, in addition to other clinical variables. Multivariable logistic regression was used to estimate adjusted odds ratios for ASCCP-congruent screening for each baseline characteristic.

**Results:** 118 women were included in the study; 38% patients were up to date per ASCCP guidelines, 16% patients were up to date per non-ASCCP guidelines, and 46% of women were overdue for screening. Having a gynecologist and being actively treated with immunosuppressant therapies were both associated with an increased odds of being up to date per the ASCCP guidelines, while Hispanic ethnicity was associated with reduced odds.

**Conclusion:** Only half of SLE women in our study had guideline-congruent cervical cancer screening. Current immunosuppression exposure, rather than SLE disease activity, was associated with an increased odds of being up to date by ASCCP guidelines. This study suggests the need for increased awareness and consensus among interdisciplinary providers regarding SLE-specific cervical cancer screening.

## INTRODUCTION

Cervical cancer is the 4<sup>th</sup> most common cancer among women and has an estimated mortality rate of 90%.<sup>1</sup> Human papillomavirus (HPV), a major driver of invasive cervical cancer, is a common infection that is particularly problematic for immunocompromised individuals due to its persistence in this population, leading to increased risk of malignant transformation. Because HPV is prevalent in the United States and is strongly linked to the development of invasive cervical cancer, it is important that immunocompromised individuals be screened regularly. HPV persistence and malignant transformation in SLE patients has been well-studied, and it is now accepted that SLE is an independent risk factor for the development of cervical intraepithelial neoplasia (CIN).<sup>2-5</sup> While SLE has not been found to be associated with increased incidence of invasive cervical cancer, this observation may be due to regular screening practices and early treatment of CIN lesions when discovered.<sup>6</sup> Importantly, SLE affects young women and disease severity is higher in ethnic minorities, which is particularly concerning, since ethnic minorities are also most at risk for cervical cancer. As of the 2020 U.S. cancer statistics report produced by the Centers for Disease Control (CDC), Hispanic and Black women ages 35 to 59 are the most likely demographic group to be diagnosed with cervical cancer.<sup>7</sup>

Despite the consensus regarding the importance of routine cervical cancer screening, there exist discordant organizational recommendations providing different cervical cancer screening schedules (**Figure 1**). Of these organizations, the American Society of Colposcopy and Cervical Pathology (ASCCP) provides the only SLE-specific guidelines for cervical cancer screening schedules; these recommendations, which are derived from those for human immunodeficiency virus (HIV) positive women, are more proactive, supporting annual cytology testing after sexual debut or starting at age 21, then extending interval cytology or co-testing (cytology and genotyping) screening to every 3 years after 3 consecutive negative cytology tests.<sup>8</sup>

Several studies suggest that women with rheumatic diseases do not receive optimal cancer screening tests and other preventative medical services, which is problematic in this patient population who is routinely exposed to immunosuppression that associates with an increased risk of virally induced cancers.<sup>9-12</sup> A variety of factors might explain this; SLE patients often have several specialty physicians as part of their care team, yet the rheumatologist may serve in a primary care role and may be unaware of SLE-specific published guidelines, specifically on cervical cancer screening. Gynecologists and primary care providers routinely perform cervical cancer screening yet may overlook or lack a familiarity of a diagnosis of SLE when risk-stratifying patients.

To investigate the cervical cancer screening practice patterns in our institution, we performed a cross-sectional study utilizing our SLE registry program to identify the adherence to the ASCCP schedule. We also aimed to identify disease-specific determinants associated with ASCCP adherence compared to those overdue for screening or to those screened per other organizational guidelines intended for the general population.

## METHODS

**Patient selection.** This was an exploratory cross-sectional study using available clinical data from patients enrolled in the University of Washington (UW) SLE biorepository program. This program is a combined longitudinal biorepository and registry, collecting patient serum samples for translational research, accompanied by clinical data on disease characteristics, disease activity and treatment at time of sample collection. Inclusion criteria were women fulfilling either the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria or the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) SLICC criteria for SLE, age between 21-65 years old, and rheumatologic care within our university system over a 5-year period (January 1, 2016 - January 1, 2021). Exclusion criteria

were patients with SLE overlap syndromes and those with an incomplete documented Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K) score, an incomplete Systemic Lupus Erythematosus Damage Index score (SDI), or missing data for more than 3 variables. Ethical approval was granted by the UW Institutional Review Board (approval number 00003007).

**Variable extraction.** The following variables were extracted from the biorepository database: patient demographics (age, race/ethnicity, educational status, insurance status), smoking status, SLE disease characteristics (date of diagnosis, 2012 or 2019 EULAR/ACR SLICC criteria met, SDI score at time of visit), comorbidities (diabetes, cardiovascular disease, kidney disease), and current and any documented prior medication exposure during the patient lifetime. Conventional disease modifying antirheumatic drugs (cDMARD) were defined by use of methotrexate, leflunomide, or sulfasalazine; immunosuppressant medications were defined by use of azathioprine, mycophenolate, or cyclophosphamide, and biologic medications were defined by use of belimumab, rituximab, or abatacept.

Chart review of the electronic medical record by two independent reviewers was performed to extract additional variables regarding healthcare factors (establishment of primary care provider and/or gynecologist, duration of follow-up with current rheumatologist and gender of rheumatologist) and gynecologic history (sexual activity, personal history of cervical cancer, personal history of cervical dysplasia, HPV vaccination status, prior history of sexually-transmitted infection (STI), current HIV status, and contraceptive use at time of visit). All available cytology, HPV genotype testing, colposcopy reports, and cervical tissue pathology reports were extracted and reviewed. Patients were categorized based on the organization guideline that best matched their cervical cancer screening schedule: ASCCP, United States Preventative Services Task Force (USPSTF), American College of Obstetrics and Gynecology (ACOG), or the American Cancer Society (ACS), (**Figure 1**). We also utilized any available

narrative from provider notes to assist in the categorization of organizational guideline screening per patient.

**Statistical analysis.** Prevalence of baseline patient characteristics among guideline strata was summarized using descriptive statistics: frequency and percentage for categorical variables, median and interquartile range (IQR) for continuous variables. For statistical analyses of the association between baseline patient characteristics and degree of guideline congruence, the categories ACOG and Overdue were combined into a single category re-labeled “Non-ASCCP,” signifying that the ASCCP guidelines were not met (patients who met the USPSTF and ACS criteria by definition also met ACOG criteria and had thus been included in the ACOG group, refer to **Figure 1**). Univariable logistic regression was used to estimate the crude odds ratio (OR) for ASCCP congruent screening for each baseline characteristic, with 95% confidence intervals and significance tests of the null hypothesis of “no association” (i.e. OR = 1). Univariable results, combined with clinical judgement, were used to identify a set of characteristics for multivariable modeling and included: Hispanic ethnicity, gynecologist (Y/N), history of nephritis (Y/N), SLEDAI-2k total score, current steroid use (Y/N), and current immunosuppressant and/or biologic use (Y/N). Multivariable logistic regression was used to estimate adjusted odds ratios for ASCCP-congruent screening for each baseline characteristic, with 95% confidence intervals and significance tests of the null hypothesis of “no association” (i.e. OR = 1). P values <0.05 were considered statistically significant. All analyses were conducted in Stata/SE Version 16 for Windows.

## RESULTS

130 women with SLE met our eligibility criteria. There were 12 women for whom screening status could not be determined from the data available and were excluded, resulting in a final sample of 118 women. The median age (IQR) was 37 (16) years, and 47% self-reported race as non-White.

95% met 2019 EULAR/ACR SLICC classification criteria for SLE; 5% met the 2012 SLICC classification criteria for SLE. Mean SLEDAI-2k score (SD) was 5.5 (5.3). Roughly one-third (36%) of the cohort had a history of biopsy-proven nephritis. 90% were on hydroxychloroquine therapy; 44% were on oral corticosteroids (equivalent to prednisone  $\geq$  5 mg daily), and 5% were receiving biologic therapy (rituximab or belimumab). Mycophenolate (39%) and methotrexate (20%) were the most common steroid-sparing agents utilized in these patients.

The majority of patients had a primary care provider (94%); only a third (33%) had a gynecology provider. 58% of women had been followed by the same rheumatologist for at least 1 year or more, and there was 50% gender congruency between patient and rheumatology provider.

**Table 1** shows baseline patient and disease factors stratified by guideline-congruent cervical cancer screening. 38% of the cohort was up to date on cervical cancer screening per ASCCP guidelines. 16% were up to date per non-ASCCP guidelines for the general population, and 46% were overdue by any organizational guideline.

Patients without a gynecologist were more likely to be overdue for screening per any guideline versus screened per ASCCP or ACOG guidelines ( $p<0.05$ ) (**Table 1**). Additionally, patients of Hispanic ethnicity tended to be overdue for screening (35%,  $p=0.04$ ). Median SLEDAI-2k and SDI scores were similar among the groups; however, a higher proportion (67%) of women screened per ASCCP guidelines were on immunosuppressant therapy compared to conventional DMARDs (16%) and biologics (7%). Women who were screened per ASCCP guidelines also had a higher proportion of having a gynecologist (51%), having been a current or former tobacco smoker (31%), had known cardiovascular disease (20%), and had documented completion of the HPV vaccination series (73%).

Univariable analyses showed that Hispanic ethnicity was associated with a reduced odds (OR 0.3, 95% CI 0.1-0.9) of being screened per ASCCP guidelines (**Table 2**). Having a gynecologist (OR 3.2, 95% CI 1.4-7.0) and being on corticosteroids or immunosuppressant therapy was

associated with an increased odds (corticosteroids OR 2.1, 95% CI 1.0-4.5; immunosuppressant therapy OR 3.0, 95% CI 1.4-6.6) of being screened per ASCCP guidelines. Results of the multivariable analyses are shown in **Table 3**. Hispanic ethnicity was associated with a reduced odds (OR 0.3, 95% CI 0.1-1.0) of being screened per ASCCP guidelines. Having a gynecologist was associated with 3-fold higher odds (OR 3.3, 95% CI 1.3-8.2) of being screened per ASCCP guidelines. Being on immunosuppressant therapy was associated with a 3-fold higher odds (OR 3.3, 95% CI 1.3-8.2) of being screened per ASCCP guidelines. SLE disease activity, damage indices, and history of renal involvement were not found to be associated with ASCCP guideline adherence.

## DISCUSSION

We observed that among SLE patients enrolled in our registry program, only half (54%) were up to date on cervical cancer screening at the time of her last rheumatology visit per any organizational guideline, and only 38% were up to date per ASCCP SLE-specific guidelines. These outcomes reflect published findings that suggest women with SLE are not receiving adequate cervical cancer screening.<sup>9-12</sup> Additionally, of those screened, roughly a third (29%) of SLE patients were screened per non-ASCCP organizational guidelines meant for the general population.

The reduced odds of cervical cancer screening among patients of Hispanic ethnicity is alarming, particularly given data that suggests increased severity and mortality due to SLE factors alone in this ethnic group.<sup>16-17</sup> This finding was not influenced by insurance status or highest educational level in the multivariate analysis. Additional measures of socioeconomic factors, such as employment status or number of dependents, were not available and thus could not be accounted for in our analyses.

In this cohort, current use of immunosuppressant and biologic medications (namely cyclophosphamide, mycophenolate, azathioprine, rituximab, belimumab, and abatacept) was

associated with 3-fold higher odds of being up to date per ASCCP guidelines, thus suggesting that immunosuppression, rather than disease activity or characteristics, may be prompting providers, largely gynecologists, to utilize ASCCP guidelines for SLE patients.

We had hypothesized that patients with high disease activity as measured by SLEDAI-2K scores might have an increased odds of more aggressive cervical cancer screening, yet this was not found to be the case in this study. In fact, SLE disease activity, damage indices, and history of renal involvement were not found to be associated with ASCCP guideline adherence. The mean SLEDAI-2K and SDI scores of the cohort correlate with low-moderate disease activity and little irreversible damage from SLE disease and treatment. It is possible that these scores were suppressed due to concomitant immunosuppressive therapy.

There is a dearth of publications that examine cervical cancer screening practices among SLE patients on immunosuppression. One recent study by Bruera et al utilized a large claims database over a 13-year period, showing that cervical cancer screening rates were higher in women with SLE (73.3%) compared to a general population cohort (58.5%) and a diabetes mellitus cohort (56.2%).<sup>10</sup> The use of claims data is limited to patients with private employer-sponsored insurance; however, the study still found that over 25% of SLE patients had not had a diagnosis or procedure code for cytology or HPV testing within 1 year prior- and 2 years post-lupus claim. Corticosteroid and immunosuppressant use were associated with a reduced odds of having had cytology or HPV testing at time of lupus claim. This contrasts to our findings, which show an increased likelihood of screening frequency in patients on immunosuppressant therapy.

The ASCCP SLE-specific guidelines were formally published in 2019, yet we found that patients followed screening schedules that aligned with these guidelines even prior to 2019. We suspect that the 2012 ASCCP guidelines, which were the first to provide risk-stratified recommendations, outlining more frequent screening for “immunosuppressed individuals” (defined by history of solid organ transplant and HIV positive status), continued to influence

gynecology providers. This would situate well with the finding that the likelihood of ASCCP guideline adherence was increased with current immunosuppression use, rather than SLE disease-specific factors. By using a study period of 2016 through 2021, it is possible that our data might mispresent low screening rates of ASCCP. However, the majority of screening status data points were taken from visits 2019 and onward (ASCCP 33/45 (73%); non-ASCCP 47/73 (64%)).

Limitations of this study include the small sample size as well as the potential for selection bias due to the utilization of a well-curated cohort. These SLE patients tend to be engaged in rheumatologic care, with visit frequency averaging every 3 months. We did not extract other variables regarding socioeconomic status beyond education and insurance status. We did not include pregnancy history in the analyses, which could influence the exposure to obstetrics/gynecology care. While we did include data regarding prior medication exposure, we did not calculate total lifetime dose exposures to DMARD, immunosuppressive, or biologic agents, acknowledging that cumulative exposure to immunomodulatory agents likely increases the risk for cervical dysplasia. Since this was an exploratory study, we did not compare this SLE cohort with a control cohort (general population) or a cohort with an analogous immunosuppressive risk (i.e. solid organ transplant or HIV). Such studies examining screening practice patterns among a larger, more diverse cohort of SLE patients should be performed to reiterate these findings and identify barriers to screening in this patient population.

Strengths of this study include the granularity of the data available regarding SLE disease factors in women with consistent rheumatologic care as well as access to SLEDAI-2K and SDI scores, which provide an individualized context of disease activity and burden when considering cervical cancer screening status. Manual chart review to determine screening status allowed for accurate documentation of which organizational screening pattern was met. Since a variety of potential outcomes are possible within a patient's lifetime (i.e., transition to dysplasia, need for colposcopy, subsequent HPV genotype testing, resolution or progression of dysplasia), the

measured outcome (which organizational screening pattern was met) likely could only be collected in this manner.

This study demonstrates the inadequate rate of disease-specific cervical cancer screening, even in an academic setting and suggests that it is the immunosuppression exposure, rather than disease activity markers, that associates with an increased odds of being screened per ASCCP guidelines. This relatively poor rate of adherence to screening guidelines is particularly important in the setting of recent approval and adoption of primary HPV genotype screening, which is increasingly promoted in the general population, but inadequate for SLE patients. These findings suggest the need for interventions to increase awareness and collaborative care among rheumatologists, primary care providers, and gynecologists regarding the ASCCP SLE-specific screening guideline schedule to ultimately enhance the quality of care of our patients.

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**Figure 1.** Summary of published organizational guidelines for cervical cancer screening in the United States. USPSTF and ACOG are directed to the general population; ASCCP guidelines are specific to systemic lupus erythematosus (SLE) regardless of immunosuppressive therapy and rheumatoid arthritis (RA) on immunosuppressive therapy.

	<b>ACS<sup>15</sup></b>	<b>USPSTF<sup>13</sup></b>	<b>ACOG<sup>14</sup></b>	<b>ASCCP<sup>8</sup></b>
<b>Cytology</b>	Every 3 years	Every 3 years	Every 3 years	Every 1 year after sexual debut or age 21; then every 3 years if consecutive normal cytology x 3
<b>Cytology + HPV (co-test)</b>	Every 5 years	Every 5 years	Every 5 years	Every 3 years if both negative; if HPV positive, then repeat co-test at 1 year (if either abnormal at that time, then colposcopy is recommended) <u>OR</u> HPV genotypes should be obtained
<b>HPV genotypes 16 &amp; 18</b>	Age ≥ 30, every 5 years; preferred over cytology alone or co-testing;	Age ≥ 30, every 5 years	Age ≥ 25, every 3 years	If 16 or 18 positive, then colposcopy is recommended; if negative, then repeat co-test in 1 year (and if either are positive, then colposcopy is recommended).

**ACS:** American Cancer Society; **USPSTF:** US Preventative Services Task Force; **ACOG:** American College of Obstetrics/Gynecology; **ASCCP:** American Society for Colposcopy and Cervical Pathology

<b>Table 1.</b> Baseline patient characteristics stratified by guideline-congruent cervical cancer screening (n=118)				
	<b>ASCCP</b>	<b>Non-ASCCP</b>	<b>Overdue</b>	<b>p value</b>
	<b>N=45</b>	<b>N=19</b>	<b>N=54</b>	
<b>Demographic data</b>				
Age, median (IQR)	35 (16)	36 (12)	41 (16)	0.61
Non-white race (%)	19 (42)	9 (47)	27 (50)	0.78
Hispanic ethnicity (%)	6 (13)	4 (21)	19 (35)	0.04
<b>Healthcare factors</b>				
Has a primary provider (%)	44 (98)	18 (95)	49 (91)	0.30
Has a gynecologist (%)	23 (51)	9 (47)	9 (17)	<0.001
Rheumatologist is female (%)	22 (49)	11 (58)	26 (48)	0.75
Duration of care with rheumatologist ≥ 1 year (%)	27 (60)	12 (63)	30 (56)	0.82
<b>Comorbidities</b>				
Current or former tobacco smoker (%)	14 (31)	3 (16)	10 (19)	0.25
Diabetes mellitus (%)	4 (9)	1 (5)	6 (11)	0.73
Cardiovascular disease (%)	9 (20)	1 (5)	6 (11)	0.21
End stage renal disease (%)	3 (7)	2 (11)	2 (4)	0.55
<b>Gynecologic history</b>				
History of cervical cancer (%)	1 (2)	--	--	0.37
HPV vaccination completed (%)	33 (73)	1 (5)	4 (7)	0.16
Reported sexual activity, current/previous (%)	28 (62)	10 (53)	24 (45)	0.71
History of sexually transmitted infection (STI) (%)	2 (4)	2 (11)	--	0.06
<b>SLE disease characteristics</b>				
History of biopsy-proven nephritis (%)	23 (51)	4 (21)	15 (28)	0.01
SLEDAI-2K total score, median (IQR)	5 (7)	4 (8)	4 (7)	0.22
SDI total score, median (IQR)	1 (1)	0 (1)	0 (1)	0.06
<b>Current medication use</b>				
Hydroxychloroquine (%)	43 (96)	16 (84)	47 (87)	0.22

Steroids (%)	25 (56)	6 (32)	21 (39)	0.12
Conventional DMARD (%)	7 (16)	4 (21)	16 (29)	0.24
Immunosuppressant (%)	30 (67)	5 (26)	24 (44)	0.006
Biologic (%)	3 (7)	--	3 (6)	0.33
<b>Prior medication exposure</b>				
Steroids (%)	11 (24)	7 (37)	22 (41)	0.22
Immunosuppressant (%)	14 (31)	6 (32)	14 (26)	0.82
Biologic (%)	5 (11)	1 (5)	4 (7)	0.69

Abbreviations: ASCCP: American Society of Colposcopy and Cervical Pathology; ACOG: American College of Obstetrics and Gynecology; HPV: human papillomavirus; SLE: Systemic Lupus Erythematosus; SLEDAI-2K Systemic Lupus Erythematosus Disease Activity Index-2000; SDI: Systemic Lupus Erythematosus Damage Index; DMARD: disease modifying antirheumatic drug  
 Conventional DMARD: methotrexate, leflunomide, sulfasalazine  
 Immunosuppressant: azathioprine, mycophenolate, cyclophosphamide  
 Biologic: belimumab, rituximab, abatacept

<b>Table 2.</b> Univariate analysis to identify predictors for meeting ASCCP screening (n=118)				
	<b>Met ASCCP screening</b> <b>Yes (%)</b> n=45	<b>No (%)</b> n=73	<b>OR</b> (95% CI)	<b>p value</b>
<b>Demographic data</b>				
Hispanic ethnicity	6 (13)	23 (32)	0.34 (0.12, 0.91)	0.03
<b>Healthcare factors</b>				
Has a gynecologist	23 (51)	18 (25)	3.19 (1.44, 7.0)	0.004
<b>Comorbidities</b>				
Never smoker	31 (69)	60 (82)	0.48 (0.20, 1.15)	0.10
Cardiovascular disease	9 (20)	7 (10)	2.36 (0.81, 6.86)	0.11
<b>Gynecologic history</b>				
HPV vaccination completed	33 (73)	56 (77)	3.05 (0.94, 9.89)	0.06
<b>SLE disease characteristics</b>				
History of nephritis class II or V	8 (18)	6 (8)	2.30 (0.74, 7.16)	0.15
History of nephritis class III or IV	15 (33)	13 (18)	2.19 (0.92, 5.20)	0.07
SLEDAI-2K total score, median (IQR)	5 (7)	4 (8)	1.06 (0.99, 1.14)	0.10
SDI total score, median (IQR)	1 (1)	0 (1)	1.27 (0.90, 1.81)	0.17
<b>Current medication use</b>				
Hydroxychloroquine	43 (96)	63 (86)	3.41 (0.71, 16.4)	0.08
Steroids	25 (56)	27 (37)	2.13 (1.00, 4.53)	0.048
Conventional DMARD	7 (16)	20 (27)	0.49 (0.19, 1.27)	0.13
Immunosuppressant	30 (67)	29 (40)	3.03 (1.40, 6.60)	0.004
Biologic	3 (7)	3 (4)	1.67 (0.32, 8.64)	0.002
<b>Prior medication exposure</b>				
Steroids	11 (24)	29 (40)	0.49 (0.21, 1.12)	0.08

Abbreviations: ASCCP: American Society of Colposcopy and Cervical Pathology; SLE: Systemic Lupus Erythematosus; SLEDAI-2K Systemic Lupus Erythematosus Disease Activity Index-2000; SDI: Systemic Lupus Erythematosus Damage Index; DMARD: disease modifying antirheumatic drug  
Conventional DMARD: methotrexate, leflunomide, or sulfasalazine  
Immunosuppressant: azathioprine, mycophenolate, cyclophosphamide  
Biologic: belimumab, rituximab, abatacept

**Table 3.** Multivariate analysis\* producing an odds ratio for meeting ASCCP screening criteria†

	Met ASCCP screening		OR (95% CI)	p value
	Yes (%) n=45	No (%) n=70		
Demographic data				
Hispanic ethnicity	6 (13)	23 (33)	0.34 (0.11, 1.01)	0.05
Healthcare factors				
Has a gynecologist	23 (51)	18 (26)	3.26 (1.30, 8.15)	0.01
SLE disease characteristics				
History of nephritis	21 (47)	16 (23)	2.13 (0.81, 5.56)	0.12
SLEDAI-2K total score, median (IQR)	5 (7)	4 (8)	1.04 (0.95, 1.14)	0.40
Current medication use				
Steroids	25 (56)	27 (39)	1.34 (0.52, 3.46)	0.55
Immunosuppressant and/or biologics	32 (71)	29 (41)	3.31 (1.34, 8.17)	0.01

\*Logistic regression model adjusted for: Hispanic ethnicity, gynecologist (Y/N), history of nephritis (Y/N), SLEDAI-2k total score, current steroid use (Y/N), and current immunosuppressant and/or biologic use (Y/N)

†Total observations n=115; n=3 omitted from analysis due to lack of data regarding history of nephritis)

Abbreviations: ASCCP: American Society of Colposcopy and Cervical Pathology; SLE: Systemic Lupus Erythematosus; SLEDAI-2K Systemic Lupus Erythematosus Disease Activity Index-2000

Conventional DMARD: methotrexate, leflunomide, or sulfasalazine

Immunosuppressant: azathioprine, mycophenolate, cyclophosphamide

Biologic: belimumab, rituximab, abatacept