

Sociodemographic Factors Associated with Pap Test Adherence and Cervical Dysplasia in Surgically Sterilized Women

Katherine C. Whitehouse¹, Jane R. Montealegre^{2,3}, Michele Follen^{4,5}, Michael E. Scheurer^{2,6}, Kjersti Aagaard^{1,7*}

1- Department of Obstetrics and Gynecology, General Division, Baylor College of Medicine, Houston, Texas, USA

2- Dan L. Duncan Cancer Center, Baylor College of Medicine, Houston, Texas, USA

3- Division of Epidemiology, Human Genetics, and Environmental Sciences, University of Texas School of Public Health, Houston, Texas, USA

4- Department of Obstetrics and Gynecology School of Medicine, Philadelphia, Pennsylvania

5- Center for Women's Health Research Drexel University, School of Medicine, Philadelphia, Pennsylvania, USA

6- Department of Pediatrics, Division of Hematology-Oncology, Baylor College of Medicine, Houston, Texas, USA

7- Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Baylor College of Medicine, Houston, Texas, USA

Abstract

Background: Routine dysplasia screening decreases the rates of cervical cancer. Since many women seek gynecological care to secure contraception, it was hypothesized that sterilized women will be less likely to undergo routine cervical cancer screening. Prior studies tried to evaluate this relationship, but results were conflicting. The study sought to further explore the sociodemographic and behavioral risk factors that might predispose sterilized women to be screening non-adherent and more likely to have cervical dysplasia.

Methods: Secondary analysis of women (n=1688) enrolled in a cross-sectional study in North America and divided into screening (n=925) and diagnostic (n=763) groups was performed. Information about sociodemographic and behavioral risk factors, surgical sterilization and date of last Pap test were obtained from questionnaires. Cervical histology was obtained from pathology records. Univariable analyses identified differences in risk factors between groups. Multivariable logistic regression models were constructed to evaluate Pap adherence and cervical dysplasia.

Results: Sterilized women were 39% more likely to be screening non-adherent ($p \leq 0.05$) especially if divorced, separated or widowed (OR=1.62), Hispanic (OR=1.57) and with a higher number of vaginal births (OR=2.00). Education was an effect measure modifier, significantly associated with non-adherence (OR=1.60). The association between sterilization and non-adherence remained significant when adjusted for confounders (AOR=1.47). Sterilization was associated with an 80% increased odds of cervical dysplasia in women over 40.

Conclusion: Sterilized women with certain sociodemographic factors are more likely to be non-adherent with Pap screening and more prone to dysplasia. These findings may assist practitioners in counseling at-risk patients.

Keywords: Cervical dysplasia screening, Pap test cervical dysplasia, Sterilization, Tubal ligation.

To cite this article: Whitehouse KC, Montealegre JR, Follen M, Scheurer ME, Aagaard K. Sociodemographic Factors Associated with Pap Test Adherence and Cervical Dysplasia in Surgically Sterilized Women. *J Reprod Infertil.* 2014;15(2):94-104.

* Corresponding Author:

Kjersti M. Aagaard,
Baylor College of
Medicine 1 Baylor Plaza,
Jones 314 Houston, TX,
77030
E-mail:
aagaardt@bcm.tmc.edu

Received: Nov. 17, 2013

Accepted: Mar. 11, 2014

Introduction

Papanicolaou dysplasia screening has been shown to decrease the mortality rate and incidence of cervical cancer by 70% since its

advent in 1941 (1-3). In resource limited settings where dysplasia screening is currently not performed, cervical cancer still remains the second

leading cause of death in women (4). Even in the US, the American Cancer Society estimated that there would be 12,170 new diagnoses of cervical cancer and 4,220 related deaths in 2012 (4, 5). Strict adherence to routine screening, proper intervention and HPV vaccination are critical to decrease the incidence (6, 7).

Surgical sterilization is a highly effective and popular contraceptive method. In the US, approximately one million adults undergo sterilization every year with an estimated 27% of women relying on tubal ligation as their primary method of contraception (8). Although sterilization is beneficial for family planning, it may negatively affect the likelihood of routine presence of women for gynecological screening since many women are motivated to seek care for obtaining birth control. It was hypothesized that surgically sterilized women will be less likely to adhere to routine dysplasia screening guidelines and it will result in higher rates and more severe cervical dysplasia. It is believed that this hypothesis would particularly be applied to populations with limited access to health care and insurance, such as the marginalized, undocumented, immigrant populations seen in large urban settings (9).

The existing literature on this subject matter is limited and conflicting. Prior studies have failed to establish a convincing or consistent relationship between surgical sterilization and cervical dysplasia or cancer (10-14). Given the conflicting and varying data available, this study sought to employ a well-characterized and robust data set of women undergoing diagnostic screening for cervical dysplasia (15-17). The purpose of this secondary analysis was to evaluate whether women with a history of surgical sterilization were less likely to be adherent with screening for dysplasia, and determine whether this can be translated into an increased prevalence of cervical dysplasia.

Methods

Data source: A cross-sectional study was performed using an epidemiological database from an established phase II clinical trial that aimed to evaluate emerging technologies for diagnosing cervical neoplasia (15-17). IRB consent was obtained from subjects for their participation in the index trial, and prior (July 31, 2011 to present) approval for research in this secondary analysis was granted from the Baylor College of Medicine IRB (H-29389). Trial participants included women with abnormal cervical cytology presenting for

colposcopy at one of three participating hospitals in the US and Canada between 1999 and 2005 (diagnostic group) as well as community volunteers with no prior history of dysplasia or cervical treatments (screening group). Cytology and histology tests were performed on all patients, as well as low and high-risk HPV types via Hybrid Capture II and PCR. Tissue biopsy was also performed and interpreted by skilled pathologists. All 1,858 subjects in the database were initially included. Cases with unknown dysplasia status, those who reported never having sexual intercourse and those with missing data regarding date of last Pap test or history of birth control use were excluded.

Measures: Sociodemographic variables in these analyses included age, race, nativity, marital status, household income, education level and employment status (18-20). Behavioral risk factors included age at first sex, number of sex partners (during past 12 months and lifetime), number of vaginal deliveries, history of oral contraceptive use, current binge drinking and current smoking (21-24). Number of vaginal deliveries was used instead of parity due to limitations of ascertainment bias and for having better accuracy. Current binge drinking was defined as consuming five or more alcoholic beverages in a single occasion more than one time in the past month.

Upon entering the study, subjects filled out a questionnaire regarding lifetime history of birth control use. Listed methods included oral contraceptives, intrauterine device, diaphragm, cream, foam/jelly/sponge, condom and surgical sterilization (25, 26). Women who used other methods were asked to specify the method and the number of years used. In this study, women with a history of surgical sterilization were defined as those who reported history of bilateral tubal ligation. Although women with no history of surgical sterilization were those who did not report receiving a bilateral tubal ligation, they did not also miss any data regarding birth control use.

Cervical cytology screening adherence was self-reported by participants on a questionnaire inquiring about date of last Pap test. Time since last cervical cytology screening was calculated as the difference between the date of the last test and the date of study enrollment. Participants were considered to be non-adherent with screening guidelines if the time duration since their cervical cytology-screening test was more than or equal to 15 months. Based on the compilation of different

guidelines from the American College of Obstetrics and Gynecology (ACOG), American Cancer Society (ACS), and US Preventative Services Task Force, it appeared that most practitioners at the time of data collection had performed annual Pap testing except "low-risk" patients with 3 consecutive negative tests (5, 25, 27, 28). Current guidelines suggest that low-risk women older than 30 years of age only need Pap screening every three years (27, 29), however, many studies have shown that the majority of practitioners in the US continue to perform annual cervical cytology screening anyway (30-32). Thus, in this study, the definition of adherence was based on the common practice of annual Pap testing.

Cervical dysplasia status was based on cytology and histology data. In cases where the diagnoses were discordant, the worst diagnosis recorded was used. For descriptive statistics, cervical dysplasia was categorized as normal (negative intraepithelial lesion, atypia, HPV-associated changes), low-grade (CIN-1, CIN-2), and high-grade (CIN-3, carcinoma in situ, invasive cancer) (33). In logistic regression analyses regarding factors associated with dysplasia, cervical dysplasia was dichotomized as normal versus other types (low- or high-grade).

Analysis: Statistical analysis was performed using Stata 12.0 software package (StataCorp, LP, College Station, TX). Descriptive statistics and chi-squared test were used to evaluate sociodemographic and behavioral risk factor differences between sterilized and non-sterilized women in both the screening and diagnostic groups. Analyses regarding surgical sterilization status and cervical cytology screening adherence were performed among screening group participants because the date of their last Pap test was independent of their enrollment in the trial. Analyses regarding surgical sterilization status and cervical dysplasia were performed among participants in the diagnostic group, in which the prevalence of cervical dysplasia was sufficiently high to evaluate the association. These analyses were further limited to US patients given the discrepancies between the US and Canadian guidelines of clinical management of cervical dysplasia (25, 34).

For both analyses, univariable logistic regression was first used to assess the crude association between surgical sterilization status and the outcome (Pap test non-adherence or cervical dysplasia). Next, multivariable logistic regression models were applied to evaluate the association between

surgical sterilization status and the respective outcome after adjusting for potential confounders. Confounders were defined as variables significantly associated with both sterilization status and the respective outcome ($p \leq 0.10$) and that changed the odds ratio by 10% or more. A p -value ≤ 0.5 was considered statistically significant.

Results

Of the initial 1,858 subjects in the database, 134 cases with unknown dysplasia status, 11 with no previous sexual intercourse, 17 with missing date of last Pap test, and 8 with missing history of birth control use were excluded. In this study, a total of 1,688 subjects with 925 in the screening group and 763 in the diagnostic group were investigated. Sociodemographic and behavioral risk factors: Of the patients in the screening group that met the study's inclusion criteria ($n=925$), 217 (23.5%) had undergone surgical sterilization (Table 1). summarizes rates of Pap test screening, sociodemographic and behavioral risk factors of the screening group in general and also based on surgical sterilization (SS) status. Regarding general sociodemographic factors, majority of subjects were white (48.65%), married (60.32%), had an income above \$40,000 (46.81%), were less educated (63.89%) but employed (68.43%). In terms of behavioral risk factors, majority had later sexual debut (63.31%), one sexual partner in the last month (75.24%), used oral contraceptive in the past (76.32%) and were not binge drinkers (58.34%) or smokers (89.84%). There were no statistically significant differences between those with and without surgical sterilization with regard to race, household income or employment status. Most women had undergone Pap test screening in the last 15 months (51.03%).

Table 1 also demonstrates that a greater proportion of women in the screening group with history of surgical sterilization were found to be non-adherent with Pap test guidelines at the time of the study: 55.3% in the surgical sterilization group versus 47% in the non-sterilization group ($p=0.028$). Non-adherence with current ACOG guidelines (27), for Pap testing every 3 years or more, was also greater among women with surgical sterilization (25.8%) compared to those without (17%). Sociodemographic variables that were significantly associated with surgical sterilization in bivariate analyses were age, marital status and education level. Specifically, patients with surgical sterilization were significantly older than their

Table 1. Cervical cancer screening, sociodemographic and behavioral risk factor characteristics by surgical sterilization status among screening group participants

	Surgical sterilization (SS)			χ^2 p-value SS v. No SS
	Overall (n=925) %	Yes (n=217) %	No (n=708) %	
Cervical cancer screening characteristics				
Last Pap test				0.028
Within past 15 months	51.03	44.70	52.97	
Within past 15 to 36 months	29.95	29.49	30.08	
Within past 36-60 months	9.41	12.90	8.33	
Over 60 months ago	9.62	12.90	8.62	
Non-adherent with screening guidelines	48.97	55.30	47.03	0.033
Sociodemographics				
Age, years				<0.001
18-30	14.16	1.84	17.94	
31-40	26.38	18.89	28.67	
41-50	29.41	41.47	25.71	
≥51	30.05	37.79	27.68	
Race				0.122
White	48.65	42.86	50.42	
Black	16.00	17.97	15.40	
Hispanic	27.68	32.72	26.13	
Other	7.68	6.45	8.05	
Marital status				<0.001
Married or living as married	60.32	65.90	58.62	
Single	18.70	7.37	22.18	
Divorced, separated, widowed	20.97	26.73	19.21	
Household income				0.437
≤\$20,000	17.73	20.28	16.95	
\$20,001-\$40,000	28.54	25.81	29.38	
≥\$40,001	46.81	48.39	46.33	
Missing	6.92	5.53	7.34	
Education				<0.001
≤High school	63.89	75.58	60.31	
>High school	36.11	24.42	39.69	
Employment status				0.676
Employed	68.43	69.59	68.08	
Unemployed	31.57	30.41	31.92	
Country of residence				0.895
United States	84.97	14.75	15.11	
Canada	15.03	85.25	84.89	
Behavioral Risk Factors				
Age at first sex, years				0.386
≤17	36.69	39.17	35.93	
>17	63.31	60.83	64.07	
Number of sex partners in past 12 months				0.974
0	18.92	19.35	18.79	
1	75.24	74.65	75.40	
≥2	5.84	5.99	5.79	
Number lifetime sex partners				0.318
1	35.57	38.25	34.75	
2-5	31.14	27.19	32.34	
≥6	28.86	31.34	28.11	
Missing	4.43	3.23	4.80	
Number vaginal deliveries				<0.001
0	41.41	27.65	45.62	
1-3	49.19	58.53	46.33	
≥4	9.41	13.82	8.05	
Ever used oral contraceptives				0.244
No	23.68	20.74	24.58	
Yes	76.32	79.26	75.40	
Current binge drinker *				0.251
No	58.34	54.38	59.60	
Yes	7.14	6.45	7.34	
Missing	34.49	39.17	33.05	
Current smoker				0.127
No	89.84	87.10	90.68	
Yes	10.16	12.90	9.32	

* Binge drinking was defined as consuming five or more alcoholic beverages in a single occasion more than one time in the past month

non-sterilized counterparts (mean 47.9 versus 42.9 years) and were more likely to be married (65.9% versus 58.6%) or divorced, separated or widowed (26.73% versus 19.2%), and to have a high school-level education or less (75.6% versus 60.3%).

Of the behavioral risk factors evaluated in this study (Table 1), only a history of vaginal delivery was significantly different between the sterilized and non-sterilized groups ($p < 0.001$). As expected, surgically sterilized women were more likely to have a higher number of vaginal births, with 13.8% having four or more vaginal deliveries and 58.53% having one to three vaginal deliveries. Among women without surgical sterilization, 8% had more than four deliveries with nearly equal proportions of the remainder having no deliveries or one to three deliveries (45.62% and 46.33%, respectively). There were no statistically significant differences between those with and without surgical sterilization with regard to their age at first sex, number of sex partners, history of oral contraceptive use, binge drinking or smoking.

Among patients in the diagnostic group ($n=763$) who met the study's inclusion criteria, 109 (14.3%) had undergone surgical sterilization. Table 2 summarizes rates of cervical dysplasia and sociodemographic and behavioral risk factors of the diagnostic group in general and based on surgical sterilization (SS) status. Overall, the subjects in the diagnostic group were mostly 18 to 40 years old (68.8%), white (63.56%), married (49.02%), had income above \$40,000 (42.33%) and were less educated (65.14%), but employed (68.02%). Regarding behavioral risk factors, most had only one sex partner in the last month (75.23%), reported more than 6 sexual partners in their life (43.91%), had ever used oral contraceptive (84.67%) and were not smokers (76.93%). 54% of subjects had normal cytology and 48% had high-risk HPV.

In table 2, prevalence of cervical dysplasia was specifically evaluated and women with surgical sterilization were more likely to have normal cytology/histology than their non-sterilized counterparts (67% vs. 52%, $p < 0.05$). The prevalence of high-grade dysplasia was equivalent among those with and without surgical sterilization (18.3% versus 18.2%). Diagnostic group patients with surgical sterilization were significantly older than their non-sterilized counterparts (41.6 versus 35.5 years with $p < 0.001$) and were more likely to be divorced, separated or widowed (40.4% versus

19.1%) and to have a high school-level education or less (83.5% versus 62.1%). Women with surgical sterilization were more likely to be black (18.3% vs. 10.2%) or Hispanic (21.1% vs. 11.3%), and more often from the US than Canada (78.1% vs. 56.3%). There were no statistically significant differences between those with and without surgical sterilization with regard to household income or employment status.

Of the behavioral risk factors evaluated in the diagnostic group (Table 2), there were significant differences between those with surgical sterilization and those without regarding age of sexual debut, number of lifetime partners and number of vaginal deliveries. As in the screening group, women with surgical sterilization were more likely to have higher parity with 18.4% having four or more vaginal deliveries (4.9%) and 66.9% having one to three vaginal deliveries (40.8%). Surgically sterilized women were more likely than non-sterilized women to have initiated sexual activity at age 17 or less (64.8% versus 53.9%), although they had fewer lifetime sexual partners, with 35.8% admitted to more than or equal to 6 partners (40.8%) among their non-sterilized counterparts. There were no statistically significant differences between those with and without surgical sterilization regarding number of partners in the last 12 months, history of oral contraceptive use, binge drinking or smoking.

Adherence with screening for dysplasia: In table 3, variables that made surgically sterilized subjects in the screening group more likely to be non-adherent to Pap test guidelines were further explored. Overall, non-adherent women were 39% more likely to be surgically sterilized than those who were adherent ($p \leq 0.05$). Women who were non-adherent were also significantly more likely to be divorced, separated or widowed (OR=1.62), Hispanic (OR=1.57) and to have had four or more vaginal deliveries (OR=2.00). They were also less likely to have a household income above \$40,000 per year (OR=0.48) or education level above high school (OR=0.62). It was found that education was an effect measure modifier of the association between surgical sterilization and screening non-adherence and therefore stratified by education level in subsequent analyses. In univariable analyses, surgical sterilization was significantly associated with non-adherence among women with a high school education or less (OR=1.60) but not among those with a higher level of education. The association between surgical sterilization and non-

Table 2. Cervical dysplasia, sociodemographic, and behavioral risk factor characteristics by surgical sterilization status among diagnostic group participants

	Surgical sterilization (SS)			χ^2 p-value SS v. No SS
	Overall (n=763) %	Yes (n=109) %	No (n=654) %	
Cervical dysplasia characteristics				
Cervical dysplasia				0.002
Normal	54.65	67.89	52.45	
Low-grade	27.13	13.76	29.36	
High-grade	18.22	18.35	18.20	
Any HPV infection	51.91	37.61	54.31	0.001
High-risk HPV infection	48.49	34.86	50.76	0.002
Sociodemographics				
Age, years				<0.001
18-30	37.61	15.60	41.28	
31-40	31.19	31.19	31.19	
41-50	18.74	35.78	15.90	
≥51	12.45	17.43	11.62	
Race				0.001
White	63.56	53.21	65.29	
Black	11.40	18.35	10.24	
Hispanic	12.71	21.10	11.31	
Other	12.32	7.34	13.15	
Marital status				<0.001
Married or living as married	49.02	54.13	48.17	
Single	28.83	5.50	32.72	
Divorced, separated, widowed	22.15	40.37	19.11	
Household income				0.121
≤\$20,000	20.48	27.52	19.42	
\$20,001-\$40,000	23.72	24.77	23.55	
≥\$40,001	42.33	33.03	43.88	
Missing	13.37	14.68	13.15	
Education				<0.001
≤High school	65.14	83.49	62.08	
>High school	34.86	16.51	37.92	
Employment status				0.975
Employed	68.02	67.89	68.04	
Unemployed	31.98	32.11	31.96	
Country of residence				<0.001
United States	59.50	78.90	56.27	
Canada	40.50	21.00	43.73	
Behavioral risk factors				
Age at first sex, years				0.036
≤17	55.51	64.81	53.98	
>17	44.49	35.19	46.02	
Number of sex partners in past 12 months				0.743
0	9.96	8.26	10.24	
1	75.23	77.98	74.77	
≥2	14.81	13.76	14.98	
Number of lifetime sex partners				0.022
1	19.66	22.02	19.27	
2-5	30.41	30.28	30.43	
≥6	43.91	35.78	45.26	
Missing	6.03	11.93	5.05	
Number of vaginal deliveries				<0.001
0	48.62	13.68	54.28	
1-3	44.56	66.97	40.83	
≥4	6.82	18.35	4.89	
Ever used oral contraceptives				0.712
No	15.33	16.51	15.14	
Yes	84.67	83.49	84.86	
Current binge drinker *				0.238
No	52.56	53.21	52.45	
Yes	20.05	14.68	20.95	
Missing	27.39	32.11	26.61	
Current smoker				0.483
No	76.93	74.31	77.37	
Yes	23.07	25.69	22.63	

*Binge drinking was defined as consuming five or more alcoholic beverages in a single occasion more than one time in the past month

Table 3. Non-adherence with cervical cancer screening guidelines by surgical sterilization status and other factors among screening group participants

	Education Level				
	Overall (n=925) OR (95% CI)	≤High school (n=591)		>High school (n=334)	
		OR (95% CI)	AOR ^a (95% CI)	OR (95% CI)	AOR ^a (95% CI)
Surgical sterilization	1.39 (1.03-1.89) **	1.60 (1.11-2.30) **	1.47 (1.00-2.15) **	0.76 (0.41-1.40)	0.87 (0.45-1.66)
Age, years					
18-30	1.00	1.00	1.00	1.00	1.00
31-40	1.20 (0.78-1.84)	1.60 (0.95-2.70) *	1.48 (0.85-2.56)	0.68 (0.32-1.42)	0.68 (0.32-1.43)
41-50		2.08 (1.23-3.50) ***	1.76 (0.99-3.13)	0.70 (0.34-1.44)	0.77 (0.36-1.64)
≥51	1.03 (0.903)	1.48 (0.88-2.49)	1.18 (0.65-2.12)	0.55 (0.27-1.11) *	0.55 (0.25-1.19)
Marital status					
Married or living as married	1.00	1.00	1.00	1.00	1.00
Single	1.17 (0.83-1.65)	1.05 (0.67-1.66)	1.37 (0.83-2.28)	1.49 (0.88-2.52)	1.30 (0.72-2.33)
Divorced, separated, widowed	1.62 (1.17-2.26) ***	1.61 (1.08-2.40) **	1.58 (1.05-2.39) **	1.41 (0.76-2.61)	1.49 (0.80-2.81)
Race					
White	1.00	1.00	--	1.00	--
Black	1.03 (0.71-1.49)	1.05 (0.67-1.65)	--	0.83 (0.42-1.64)	--
Hispanic	1.57 (1.15-2.13) ***	1.49 (1.03-2.17) **	--	1.40 (0.77-2.52)	--
Other	0.62 (0.37-1.05) *	0.66 (0.29-1.53)	--	0.68 (0.34-1.34)	--
Household income					
≤\$20,000	1.00	1.00	--	1.00	--
\$20,001-\$40,000	0.84 (0.57-1.25)	0.70 (0.44-1.12)	--	1.43 (0.66-3.10)	--
≥\$40,001	0.48 (0.33-0.69) ***	0.52 (0.33-0.82) ***	--	0.57 (0.29-1.13)	--
Employment status					
Unemployed	1.00	1.00	--	1.00	--
Employed	1.04 (0.79-1.37)	0.3 (0.66-1.32)	--	1.32 (0.82-2.14)	--
Education level					
≤High school	1.00	--	--	--	--
>High school	0.62 (0.47-0.81) ***	--	--	--	--
Number vaginal deliveries					
Zero	1.00	1.00	1.00		1.00
1 to 3	0.99 (0.75-1.30)	1.04 (0.73-1.48)	1.00 (0.69-1.47)	0.74 (0.47-1.16)	0.84 (0.50-1.40)
4 or more	2.00 (1.23-3.23) ***	1.84 (1.05-3.24) **	1.69 (0.92-30.8) *	1.85 (0.67-5.08)	2.20 (0.77-6.32)

* p<0.10, ** p<0.05, *** p<0.01

a: Adjusted for variables significantly associated with screening non- adherence and surgical sterilization status

adherence remained significant after adjusting for age, marital status, and number of vaginal deliveries (AOR=1.47).

Prevalence of dysplasia: In table 4, factors that made surgically sterilized subjects in the diagnostic group more likely to have dysplasia were evaluated. Overall, there was no association between cervical dysplasia and surgical sterilization status; however, stratified analyses indicated that among women older than 40 years, surgical sterilization

was associated with an 80% increased chance of dysplasia. This association was not statistically significant, likely due to the smaller sample size of women in these strata compared to the overall study size. The magnitude of the association did not change after adjusting for variables significantly associated with cervical dysplasia and surgical sterilization (race, marital status, education, and age of sexual debut).

Table 4. Risk of cervical dysplasia by surgical sterilization status and other factors among diagnostic group participants residing in the United States

	Age				
	Overall (n=454)	≤40 years (n=277)		>40 years (n=177)	
	OR (95% CI)	OR (95% CI)	AOR ^a (95% CI)	OR (95% CI)	AOR ^a (95% CI)
Surgical sterilization	0.87 (0.50-1.49)	0.86 (0.31-1.80)	0.75 (0.35-1.62)	1.83 (0.73-4.56)	1.81 (0.67-4.93)
Race					
White	1.00	1.00	1.00	1.00	1.00
Black	2.39 (1.41-4.05) ***	1.67 (0.91-3.08)	1.49 (0.77-2.86)	3.82 (1.23-11.85) **	2.84 (0.81-9.94)
Hispanic	1.70 (1.00-2.90) **	1.47 (0.79-2.72)	1.24 (0.65-2.39)	1.53 (0.45-5.20)	1.12 (0.31-4.14)
Other	0.92 (0.30-2.87)	0.64 (0.41-11.08)	0.70 (0.14-3.59)	2.12 (0.41-11.08)	3.11 (0.54-17.89)
Marital status					
Married or living as married	1.00	1.00	1.00	1.00	1.00
Single	1.63 (0.95-2.78) *	1.12 (0.63-2.01)	1.04 (0.56-1.91)	1.04 (0.12-9.11)	1.12 (0.12-10.64)
Divorced, separated, widowed	1.00 (0.60-1.65)	0.81 (0.42-1.56)	0.80 (0.41-1.57)	2.21 (0.89-5.47) *	1.92 (0.72-5.14)
Education level					
≤High school	1.00	1.00	1.00	1.00	1.00
>High school	0.46 (0.28-0.76) ***	0.56 (0.31-1.03) *	0.65 (0.33-1.29)	0.48 (0.18-1.29)	0.51 (0.16-1.62)
Age at first sex, years					
≤17	1.00	1.00	1.00	1.00	1.00
>17	0.63 (0.41-0.96) **	0.76 (0.45-1.28)	0.82 (0.47-1.41)	0.84 (0.34-2.02)	1.60 (0.56-4.59)
Number lifetime sex partners					
1	1.00	1.00	--	1.00	--
2-5	0.97 (0.55-1.72)	0.78 (0.38-1.59)	--	0.59 (0.18-1.91)	--
≥6	1.08 (0.62-1.88)	0.87 (0.43-1.76)	--	0.68 (0.22-2.07)	--
Current smoker	1.48 (0.90-2.41)	1.14 (0.65-2.01)	--	1.86 (0.62-5.57)	--

* p≤0.10, ** p≤0.05, *** p≤0.01

a: Adjusted for variables significantly associated with cervical dysplasia and surgical sterilization status

Discussion

Main findings: This study explored whether surgically sterilized women with certain sociodemographic risk factors were more likely to be non-adherent with cervical cytology and dysplasia screening. The data suggests that women with surgical sterilization are more likely to be non-adherent with screening guidelines, even after controlling for age, marital status, education and number of vaginal deliveries, which were found to be significantly associated with screening non-adherence. Among women over 40 years of age, the data suggest that surgical sterilization may be associated with increased prevalence of cervical dysplasia.

Although cervical cancer is presently attributed to be a disease of the developing world, evidence also suggests that increased cervical cancer morbidity and mortality in the US exists for those with decreased access to care or residing in low-

resource settings. This is notably true in areas of the US with large immigrant and underserved populations who also utilize surgical sterilization as a prevalent means of contraception (9, 18, 19).

Strengths and limitations: There were both inherent strengths and limitations to the study. A major strength of the study is its large and diverse sample size. Despite applying a convenience sampling, the large screening group was more likely indicative of the general US population than those populations examined in prior studies (10, 12-14). Data on cervical dysplasia can be considered reliable and accurate as it was based on a consensus diagnosis of cytological and histological evaluation, thus minimizing any potential misclassification resulting from using cytology alone. Moreover, this study identified education level less than or equal to a high school degree as an effect measure modifier in tubal ligation and adherence with screening. This has independent value for

practitioners and will serve as an immediate potential avenue for awareness and outreach in clinical settings.

Despite these strengths, the study was limited by the fact that the diagnostic group was a hospital-based sample while the screening group was a convenience sample. While inferences can be drawn from these data, a true cause and effect relationship between non-adherence with Pap tests and increased cervical dysplasia in a single population cannot be shown. In addition, as the study's database only included history of number of vaginal deliveries and had no information about the number of Cesarean deliveries, this limited the ability to evaluate the association of true parity and the outcomes (although it can be well approximated given the overall low rate of Primary Cesarean in the cohort). Since complete medical chart of each patient was not available, date of last Pap test and surgical sterilization status were based on self-report and thus subject to recall bias. Prior studies have suggested that there may be a temporary protective effect of surgical sterilization on cervical cancer risk due to pre-operative screening routines (11, 12). Unfortunately, historical dates of surgical sterilization were not available and therefore it was not possible to draw any temporal relationships between sterilization and date of last Pap test or date of dysplastic lesions. Finally, the definition of non-compliance was not based on today's ACOG guidelines for less frequent screening as the study chose to evaluate the data based on guidelines current at the time the study was conducted. (27, 28). However, the link between surgical sterilization and adherence with Pap testing was evaluated every 3 years and findings were similarly striking for decreased adherence between both screening regimens.

Conclusion

Despite limitations, the findings suggest that women with surgical sterilization are more likely to be non-adherent with screening guidelines, even after controlling for age, marital status, education, and number of vaginal deliveries. Among women over 40 years of age, the data suggest that surgical sterilization may be associated with increased prevalence of cervical dysplasia. Most importantly, in this study, there was a population of women who were at risk for cervical dysplasia and potentially poor in adhering to the follow-up regimen accepted at the time of database creation. Because this study is only an exploratory one, fu-

ture analyses might further identify at-risk cohorts and guide practitioners in improving patient education about routine gynecological follow-ups for cervical dysplasia screening at the time of sterilization. It would be advantageous to perform a comparable analysis in a developing country to ascertain whether similar risk factors exist where cervical cancer is even more common. While the findings in this study have meaningful implications to women's health, they are yet to be fully realized. It is hoped that these findings will serve as an impetus for further research to strengthen and expand upon what is a novel arena for reducing cervical cancer risk.

Acknowledgement

The data presented in this analysis were collected as part of P01CA082710 (M. Follen PI).

Conflict of Interest

The authors report no commercial or conflicting interests to disclose. The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the Cancer Prevention and Research Institute of Texas.

References

1. DiSaia P, Creasman W. Clinical gynecologic oncology. 7th ed. Philadelphia, PA: Elsevier; 2007.
2. Mathew A, George PS. Trends in incidence and mortality rates of squamous cell carcinoma and adenocarcinoma of cervix--worldwide. *Asian Pac J Cancer Prev*. 2009;10(4):645-50.
3. American Cancer Society. What are the key statistics about cervical cancer? [Internet]. Atlanta, GA: American Cancer Society; 2014 [updated 2014; cited 2014 Feb 6]. Available from: <http://www.cancer.org/cancer/cervicalcancer/detailedguide/cervical-cancer-key-statistics>
4. Waggoner SE. Cervical cancer. *Lancet*. 2003;361(9376):2217-25.
5. American Cancer Society. Cancer Prevention & Early Detection Facts & Figures 2012 [Internet]. Atlanta, GA: American Cancer Society; 2012 [updated 2014; cited 2014 Feb 6]. Available from: http://www.cancer.org/acs/groups/content/@epidemiology_surveillance/documents/document/acspc-033423.pdf.
6. Martin CK, Richardson LC, Berkman ND, Kuo TM, Yuen AN, Benard VB. Impact of the 2002 American society for Colposcopy and Cervical Pathology guidelines on cervical cancer diagnosis in a geographically diverse population of commercially in-

- sured women, 1999-2004. *J Low Genit Tract Dis.* 2011;15(1):25-32.
7. Stanley M. Pathology and epidemiology of HPV infection in females. *Gynecol Oncol.* 2010;117(2 Suppl):S5-10.
 8. Speroff L, Darney P. A clinical guide for contraception. 4th ed. Philadelphia, PA: Lippincott, William & Wilkins; 2005.
 9. Eggleston KS, Coker AL, Williams M, Tortolero-Luna G, Martin JB, Tortolero SR. Cervical cancer survival by socioeconomic status, race/ethnicity, and place of residence in Texas, 1995-2001. *J Womens Health (Larchmt).* 2006;15(8):941-51.
 10. Cohen MM, Roos NP. Cervical cytology screening after tubal ligation. *Am J Prev Med.* 1986;2(4): 220-5.
 11. Kjaer SK, Mellekjaer L, Brinton LA, Johansen C, Gridley G, Olsen JH. Tubal sterilization and risk of ovarian, endometrial and cervical cancer. A Danish population-based follow-up study of more than 65 000 sterilized women. *Int J Epidemiol.* 2004;33(3):596-602.
 12. Li HQ, Thomas DB, Jin SK, Wu F. Tubal sterilization and use of an IUD and risk of cervical cancer. *J Womens Health Gend Based Med.* 2000;9(3): 303-10.
 13. Winkler HA, Anderson PS, Fields AL, Runowicz CD, DeVicoria C, Goldberg GL. Compliance with Papanicolaou smear screening following tubal ligation in women with cervical cancer. *J Womens Health.* 1999;8(1):103-7.
 14. Mathews CA, Stoner JA, Wentzensen N, Moxley KM, Tenney ME, Tuller ER, et al. Tubal ligation frequency in Oklahoma women with cervical cancer. *Gynecol Oncol.* 2012;127(2):278-82.
 15. Pham B, Rhodes H, Milbourne A, Adler-Storthz K, Follen M, Scheurer ME. Epidemiologic differentiation of diagnostic and screening populations for the assessment of cervical dysplasia using optical technologies. *Gend Med.* 2012;9(1 Suppl):S36-47.
 16. Pruitt SL, Parker PA, Peterson SK, Le T, Follen M, Basen-Engquist K. Knowledge of cervical dysplasia and human papillomavirus among women seen in a colposcopy clinic. *Gynecol Oncol.* 2005;99(3 Suppl 1):S236-44.
 17. Scheurer ME, Tortolero-Luna G, Guillaud M, Follen M, Chen Z, Dillon LM, et al. Correlation of human papillomavirus type 16 and human papillomavirus type 18 e7 messenger RNA levels with degree of cervical dysplasia. *Cancer Epidemiol Biomarkers Prev.* 2005;14(8):1948-52.
 18. Coker AL, Desimone CP, Eggleston KS, White AL, Williams M. Ethnic disparities in cervical cancer survival among Texas women. *J Womens Health (Larchmt).* 2009;18(10):1577-83.
 19. Garner EI. Cervical cancer: disparities in screening, treatment, and survival. *Cancer Epidemiol Biomarkers Prev.* 2003;12(3):242s-247s.
 20. Ibfelt E, Kjaer SK, Johansen C, Hogdall C, Steding-Jessen M, Frederiksen K, et al. Socioeconomic position and stage of cervical cancer in Danish women diagnosed 2005 to 2009. *Cancer Epidemiol Biomarkers Prev.* 2012 May;21(5):835-42.
 21. MacLaughlan SD, Lachance JA, Gjelsvik A. Correlation between smoking status and cervical cancer screening: a cross-sectional study. *J Low Genit Tract Dis.* 2011;15(2):114-9.
 22. Nelson W, Moser RP, Gaffey A, Waldron W. Adherence to cervical cancer screening guidelines for U.S. women aged 25-64: data from the 2005 Health Information National Trends Survey (HINTS). *J Womens Health (Larchmt).* 2009;18(11):1759-68.
 23. Russo E, Kupek E, Zanine RM. Vaginal delivery and low immunity are strongly associated with high-grade cervical intraepithelial neoplasia in a high-risk population. *J Low Genit Tract Dis.* 2011; 15(3):195-9.
 24. Smith AM, Heywood W, Ryall R, Shelley JM, Pitts MK, Richters J, et al. Association between sexual behavior and cervical cancer screening. *J Womens Health (Larchmt).* 2011;20(7):1091-6.
 25. U.S. Preventive Services Task Force. Screening for cervical cancer: recommendations and rationale. *Am J Nurs.* 2003;103(11):101-2, 105-6, 108-9.
 26. International Collaboration of Epidemiological Studies of Cervical Cancer, Appleby P, Beral V, Berrington de González A, Colin D, Franceschi S, et al. Cervical cancer and hormonal contraceptives: collaborative reanalysis of individual data for 16,573 women with cervical cancer and 35,509 women without cervical cancer from 24 epidemiological studies. *Lancet.* 2007;370(9599):1609-21.
 27. ACOG Committee on Practice Bulletins Gynecology. ACOG Practice Bulletin no. 109: Cervical cytology screening. *Obstet Gynecol.* 2009;114(6): 1409-20.
 28. [No authors listed]. ACOG committee opinion. Recommendations on frequency of Pap test screening. Number 152--March 1995. Committee on Gynecologic Practice. American College of Obstetricians and Gynecologists. *Int J Gynaecol Obstet.* 1995;49(2):210-1.
 29. Smith RA, Brooks D, Cokkinides V, Saslow D, Brawley OW. Cancer screening in the United States, 2013: a review of current American Cancer

Society guidelines, current issues in cancer screening, and new guidance on cervical cancer screening and lung cancer screening. *CA Cancer J Clin.* 2013;63(2):88-105.

30. Roland KB, Soman A, Benard VB, Saraiya M. Human papillomavirus and Papanicolaou tests screening interval recommendations in the United States. *Am J Obstet Gynecol.* 2011;205(5):447.e1-8.
31. Saraiya M, Berkowitz Z, Yabroff KR, Wideroff L, Kobrin S, Benard V. Cervical cancer screening with both human papillomavirus and Papanicolaou testing vs Papanicolaou testing alone: what screening intervals are physicians recommending?. *Arch Intern Med.* 2010;170(11):977-85.
32. Sirovich BE, Welch HG. The frequency of Pap smear screening in the United States. *J Gen Intern Med.* 2004;19(3):243-50.
33. Wright TC Jr, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D. 2006 consensus guidelines for the management of women with cervical intraepithelial neoplasia or adenocarcinoma in situ. *Am J Obstet Gynecol.* 2007;197(4):340-5.
34. Canadian Task Force on Preventive Health Care, Pollock S, Dunfield L, Shane A, Kerner J, Bryant H, et al. Recommendations on screening for cervical cancer. *CMAJ.* 2013;185(1):35-45.