

Evaluation of a vaginal estrogen cream protocol in postmenopausal women with low grade Pap tests



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Disclosures

- No financial relationships or conflicts of interest to disclose for all authors



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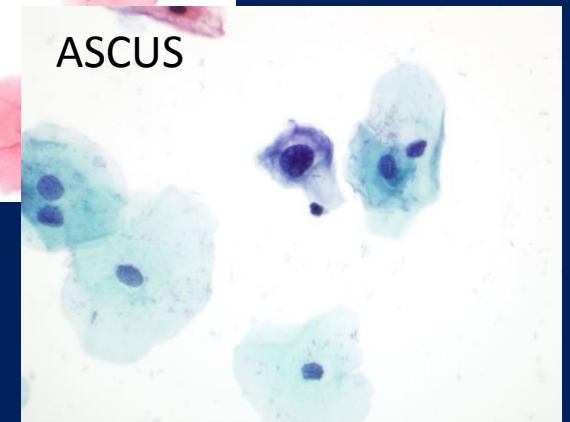
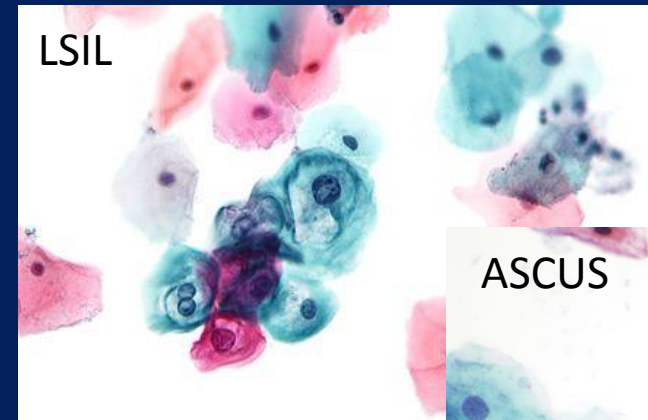
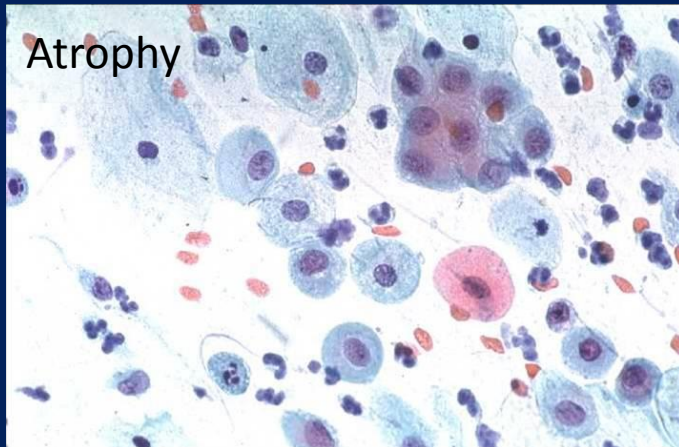


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Introduction

When screening for cervical dysplasia, the hypo-estrogenism of postmenopausal patients can mimic low grade changes and impede ability to obtain an adequate colposcopy.



Images from "Cytopathology" on glowm.com



Introduction

In controlled research settings,

- Hormone replacement normalized 84%¹, 85%² of pap tests with squamous atypia
- A three month course of vaginal estrogen cream improved the number of adequate colposcopies from 28 to 80% ²

1. Kaminski 1989 2. Piccoli 2008



Study Objective

To evaluate the completion and impact of a vaginal estrogen cream (VEC) protocol for postmenopausal women with low grade Pap tests



Methods

Approved by Colorado Multiple Institutional Review Board
Case series of prospectively-enrolled cohort
Single academic institution, Denver Health Medical Center
Between 2012 and 2016



Methods

Inclusion criteria: All postmenopausal women with atypical squamous cells of undetermined significance (ASCUS) with positive human papillomavirus (HPV +) or low grade squamous intraepithelial lesion (LSIL) Pap test results.

Exclusion criteria:

- **Prior hysterectomy**
- **Immunocompromised**
- **Incarcerated**
- **Reported allergy to VEC**
- **HIV positive**
- **Unwilling to use VEC**
- **H/o cervical cancer**



Methods: 12 week Vaginal Estrogen Cream (VEC) Protocol

Managed by two dedicated dysplasia registered nurses

Low grade
Pap test

VEC
nightly
2 weeks

VEC
3 nights/week
10 weeks

Colposcopy &
repeat Pap test

Adherence:

Self-reported 12 weeks
of VEC use as directed*

And:

Return visit

>3 months (11 weeks)
<6 months (28 weeks)

Methods

- ❖ Primary Outcome: Adherence to VEC protocol
- ❖ Secondary Outcomes: Descriptive statistics on repeat Pap tests, colposcopy findings

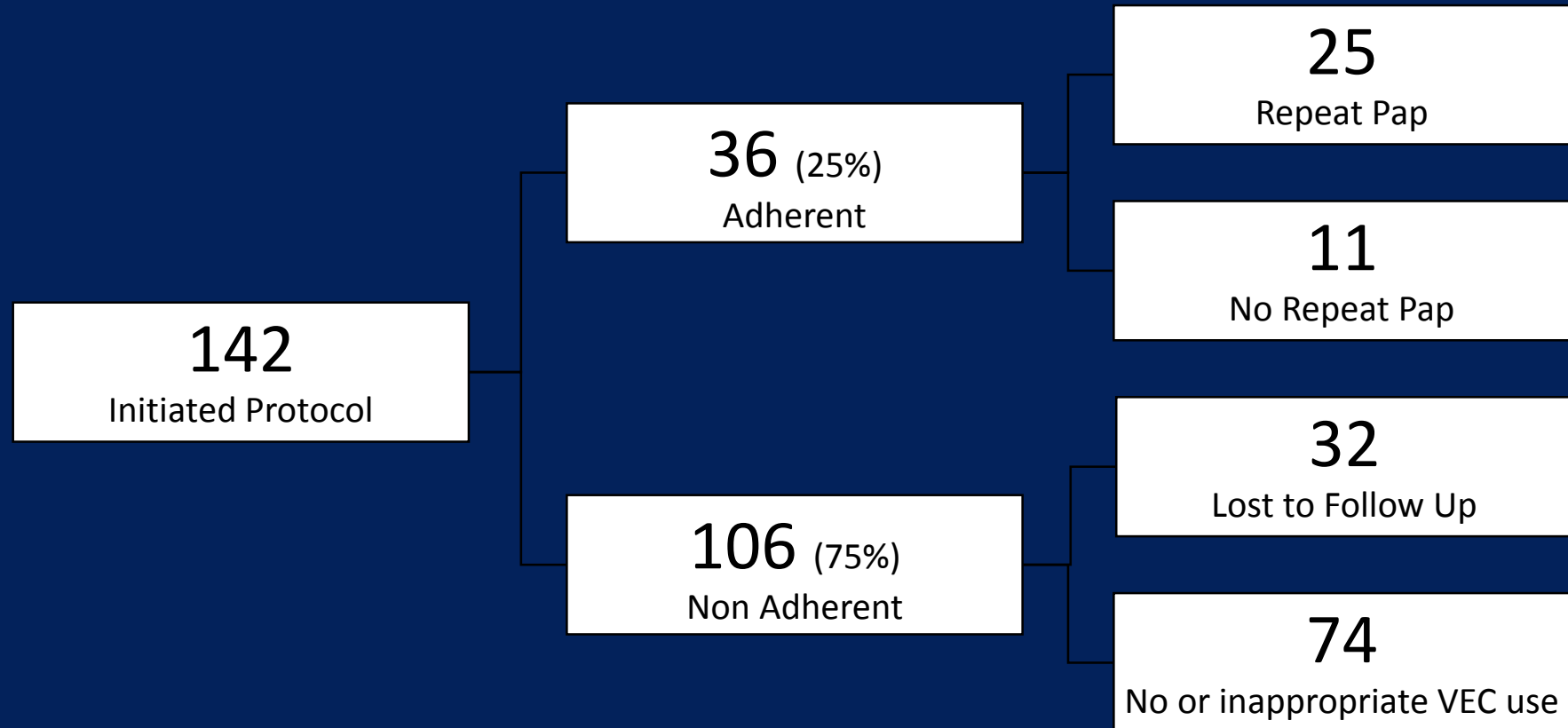


R E S U L T S

Demographic		Adherent, N=36 (%)	Non Adherent, N=106 (%)	p-value
Age	Gmean (95%GMCI)	57.1 (55.8, 58.5)	54.4 (53.2, 55.5)	0.002
Initial Pap result	ASCUS	10 (27.8)	33 (31.1)	0.834
	LSIL	26 (72.2)	73 (68.9)	
Language	English	25 (69.4)	83 (78.3)	0.366
	Spanish or Other	11 (30.5)	23 (21.7)	
Race	White	29 (80.6)	85(80.2)	0.705
	Black	4 (11.1)	16(15.1)	
	Otherwise	3 (8.3)	5 (4.7)	
Ethnicity	Hispanic	13 (36.1)	56 (52.8)	0.122
	Otherwise	23 (63.9)	50 (47.2)	
Insurance	Public or none	32 (88.9)	94 (88.7)	>0.99
	Private	4 (11.1)	12 (11.3)	
Parity	Null	3 (8.6)	8 (8.9)	>0.99
	1+	32 (91.4)	81 (91.0)	
Tobacco Use	Never	18 (50.0)	42 (40.4)	0.319
	Past	8 (22.2)	18 (17.3)	
	Present	10 (27.8)	44 (42.3)	

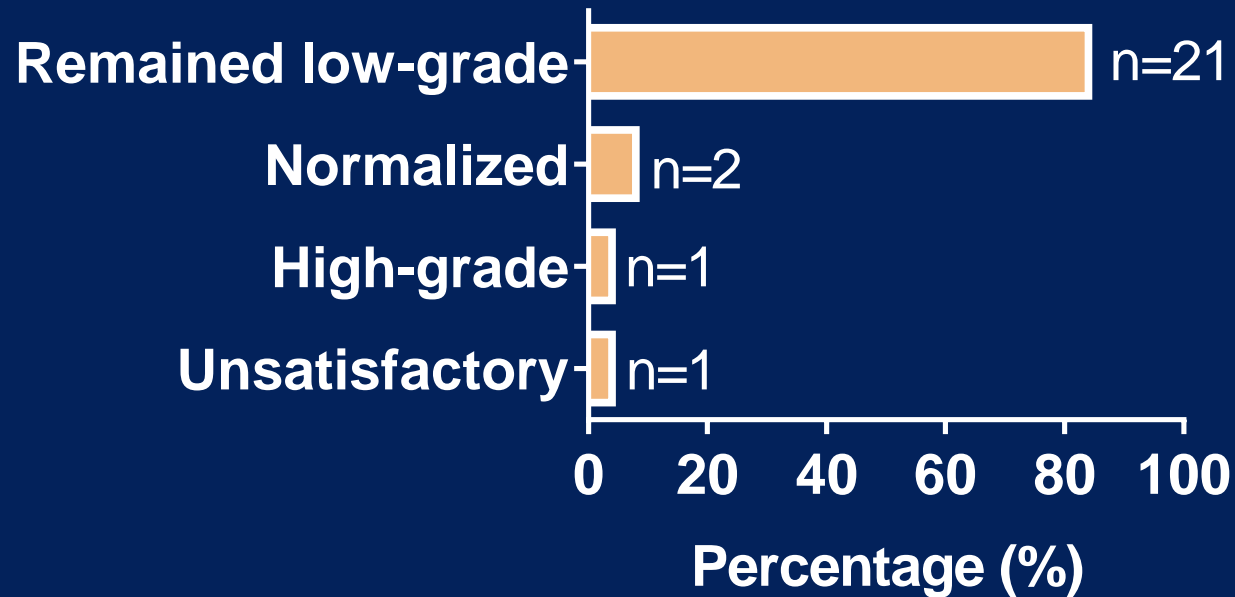


Results: Primary Outcome - Adherence



Results: Secondary Outcomes

- Of adherent patients, 69% were categorized as such because a repeat Pap test was performed, of these:



Results: Secondary Outcomes

Percentage of adequate coloscopies between adherent and non adherent groups was similar.

		Adherent, N=36 (%)	Non Adherent, N=106 (%)	p-value
Adequate colposcopy	No	25 (69.4)	48 (64.9)	0.673
	Yes	11 (30.5)	26 (35.1)	



R E S U L T S

Colposcopy Visit Outcome		Adherent, N=36 (%)	Non Adherent, N=106 (%)	p-value
Colposcopic Impression	normal	23 (67.7)	43 (58.1)	0.455
	low grade	4 (11.8)	16 (21.6)	
	high grade	0	0	
	unsatisfactory	7 (20.6)	15 (20.3)	
Number of Biopsies	Zero	9 (25.0)	20 (26.3)	>0.99
	1	20 (55.6)	40 (52.6)	
	2	6 (16.7)	14 (18.4)	
	3	1 (2.8)	2 (2.6)	
Pathology of highest grade cervical biopsy	normal	7 (25.9)	9 (16.1)	0.287
	low grade	20 (74.1)	44 (78.6)	
	high grade	0	3 (5.4)	
Pathology of endocervical sampling	normal	16 (45.7)	21 (28.4)	0.293
	low grade	17 (48.6)	48 (64.9)	
	high grade	1 (2.9)	4 (5.4)	
	unsatisfactory	1 (2.9)	1 (1.4)	



Discussion

- **This study suggests, that in the real clinical setting, adherence to a practical VEC protocol is low and does not yield the clinical outcomes others have described, including improved rates of adequate colposcopy**
- A VEC protocol may only delay colposcopic evaluation and treatment of HPV-associated dysplasia



Discussion

Strengths	Limitations
<p>Demonstrates real-life application in a safety-net hospital with high rates of dysplasia</p> <p>Dedicated dysplasia nurses with standardized follow-up.</p>	<p>Repeat Pap test collection used as surrogate for adherence</p> <p>Not powered to look at difference in our secondary outcomes</p> <p>Medical documentation not originally intended for being used for research</p> <p>Outside follow-up not assessed</p> <p>High-risk safety-net hospital limits generalizability</p>



Conclusions

In postmenopausal patients with low-grade Pap test results:

- ❖ Adherence to a 12 week VEC protocol was low
- ❖ 12 week VEC protocol was ineffective at normalizing low-grade Pap test results or impacting the adequacy of colposcopy.

These results do not support delaying follow-up colposcopy for a course of vaginal conjugated equine-estrogen cream for postmenopausal women with low grade Pap tests.



Questions?



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References

1. Kaminski PF, Sorosky JI, Wheelock JB, Stevens CW: The significance of atypical cervical cytology in an older population. *Obstet Gynecol.* 1989; 73: 13– 15.
2. Piccoli R, Mandato V, Lavitola, et al: Atypical squamous cells and low-grade squamous cell lesions in postmenopausal women: Implications for management. *Euro J Obstet Gyn and Reproductive Biology* 2008; 140.2: 269-274.

