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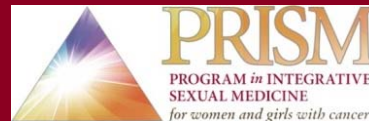


## Vaginal cytological characteristics as a biomeasure of estrogenization in a community- based population of older women

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Institute for  
Mind and Biology  
Division of the  
Social Sciences



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Chicago Core on Biomarkers in Population-Based Aging Research  
The Center on Aging at NORC and the University of Chicago

# Disclosures

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  - 1K23AG032870 (Lindau, PI)
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- The authors report no conflicts of interest

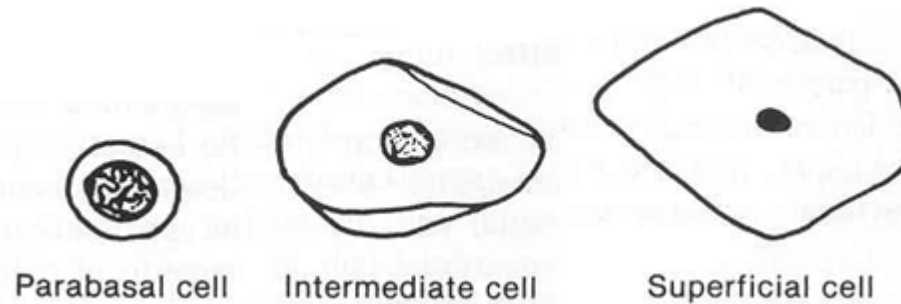
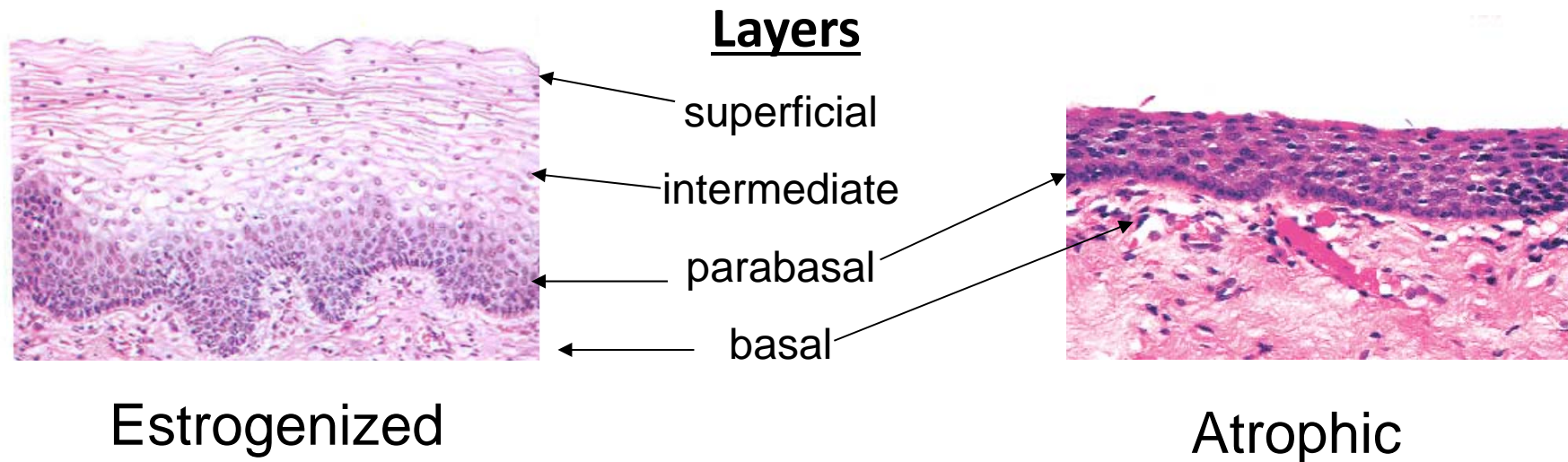


# Background

- Vaginal mucosa is a target tissue for a broad spectrum of estrogens.
- Vaginal atrophy
  - Indicates an estrogen deficit.
  - May interfere with sexual and urinary function.
  - Increases with age after menopause.



# Vaginal Epithelium

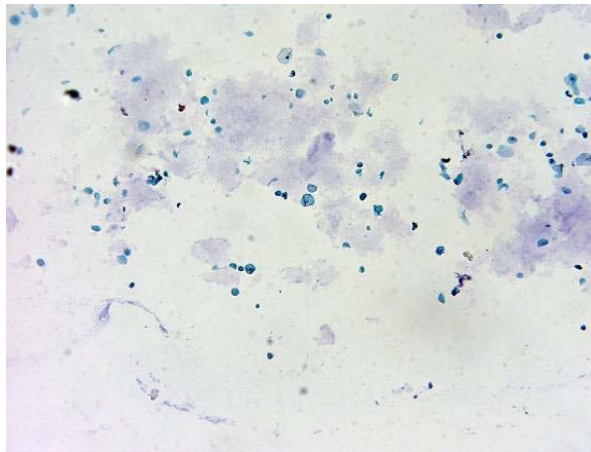


## Three Types (Or Stages) of Vaginal Epithelial Cells

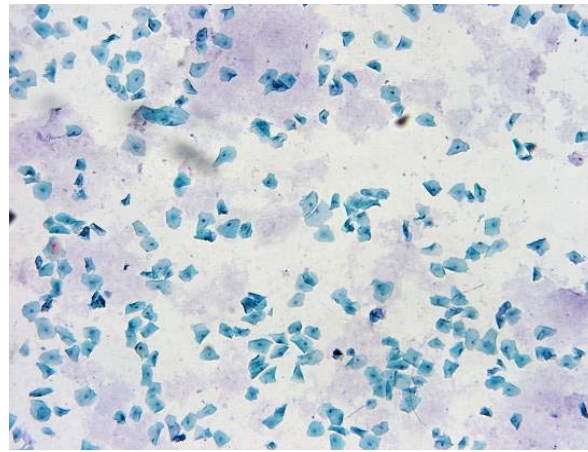
All scored to quantify estrogenization in the **Vaginal Maturation Index**

The Vaginal Maturation Index quantifies the relative proportion of the vaginal parabasal (P), intermediate (I), and superficial (S) cells presented as % P / % I / % S.

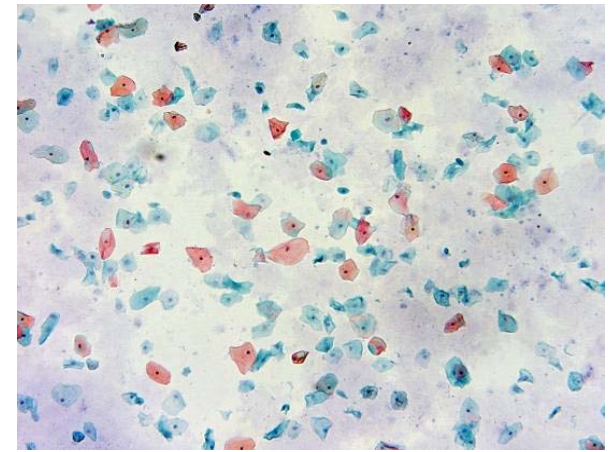
# Quantifying Types of Desquamated Vaginal Epithelial Cells



**LESS  
ESTROGENIZED**



**INTERMEDIATE**



**MORE  
ESTROGENIZED**

Multichrome Papanicolaou stained cytology specimens obtained using vaginal self-swabs in NSHAP Wave 1.

McClintock lab:

- scored number and proportion of three epithelial cell types
- created a Maturation Index (MI).



# Methods



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# National Social Life, Health and Aging Project (NSHAP) Wave 1



- Nationally representative sample of people 57 to 85 years of age (Wave 1, 2005 – 06).
- Demographic, health, sexual, physical, and biological measures collected in the home.
- Vaginal swabs were self-collected and used for the following measures:
  - Maturation Value (MV)
  - Vaginal Candidiasis (yeast)
  - Bacterial Vaginosis (BV)
  - High Risk Human Papilloma Virus (HPV)

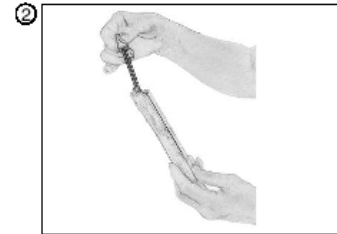
The Institutional Review Boards of the University of Chicago and the National Opinion Research Center approved the protocol; all participants provided written documentation of informed consent.

# Vaginal Swab Sample Collection

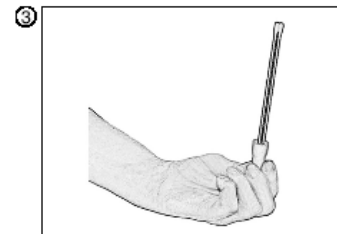
## Vaginal Swab Instructions



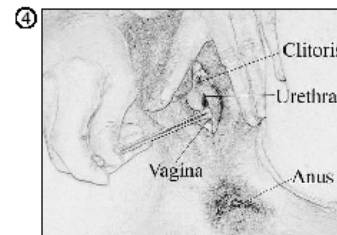
Choose a comfortable position. Either gently squat by bending at the knees, or sit on the toilet.



Remove swabs from packaging.



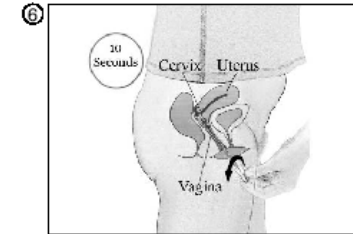
Hold swabs with the tip up. You may do all the swabs at once or one or two at a time.



Relax and gently insert the swabs into the vagina.



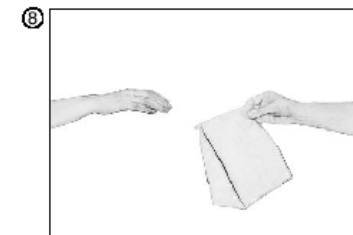
Stop when your fingers reach the vaginal opening or if you feel discomfort.



Turn the swabs inside the vagina as you count to 'ten.'



Place swabs and packaging directly inside the bag.



Return the bag to the interviewer.



Do not throw anything in the trash. Please place all packaging into the bag.

You may notice a small amount of discharge or blood on the swab. This is common and is not a cause for concern.

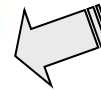
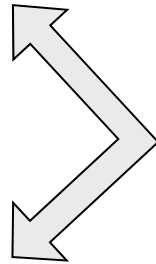
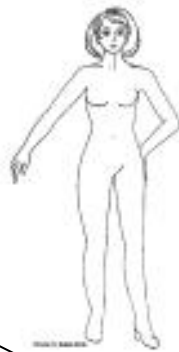
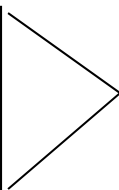
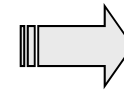
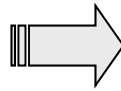
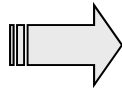


Illustrated by Rachel Seelen





July 1, 2005

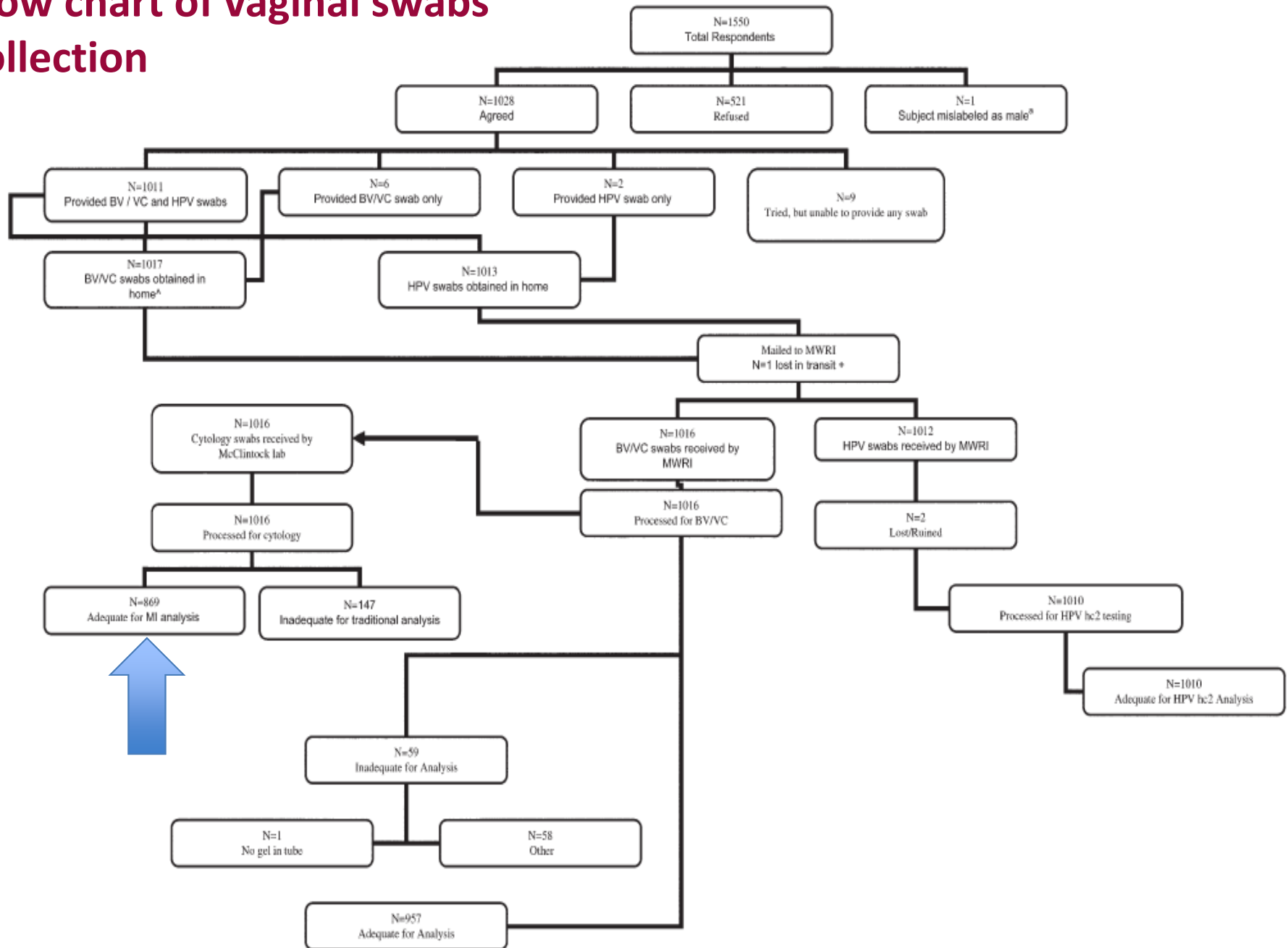


◀  
Cytopathology Lab  
University of Chicago Hospitals  
Chicago, IL  
January 2006  
Papanicolaou Stain

McClintock Lab  
Institute for Mind  
and Biology  
Chicago, IL  
July 20, 2005  
Cells from swab  
to slide,  
MI

Jordan Lab,  
Magee Women's  
Hospital Pittsburgh,  
PA  
July 6, 2005  
BV, Yeast, HPV

# Flow chart of vaginal swabs collection



## Successful Vaginal Swab Collection

- 66% of women agreed to provide a self-administered vaginal swab specimen (N = 1,028 of 1,550)
- 85% were adequate for MI scores (N = 869 of 1,028)
- Non-responders to the vaginal swab protocol were :
  - older
  - <HS graduate
  - less likely to report a recent pelvic examination, menopausal prescription hormone use

Lindau et al., 2008



**The Maturation Value  
is a clinical measure of vaginal estrogenization  
derived from the Maturation Index**

Maturation Value =

1.0 x % superficial cells +

0.5 x % intermediate cells +

0.0 x % parabasal cells

Potential range: 0 – 100



# Maturation Value of the Vaginal Epithelium

- suggested by Meisels in Acta Cytologica, 1965, who called it an “estrogenic value”
- a bioassay of functionally active estrogens counteracted by progesterone
- provides an integrated measure of hormonal bioactivity over many days
- based only on intermediate and superficial epithelial cells



# Hypotheses

Vaginal epithelial estrogenization among post-menopausal women will be:

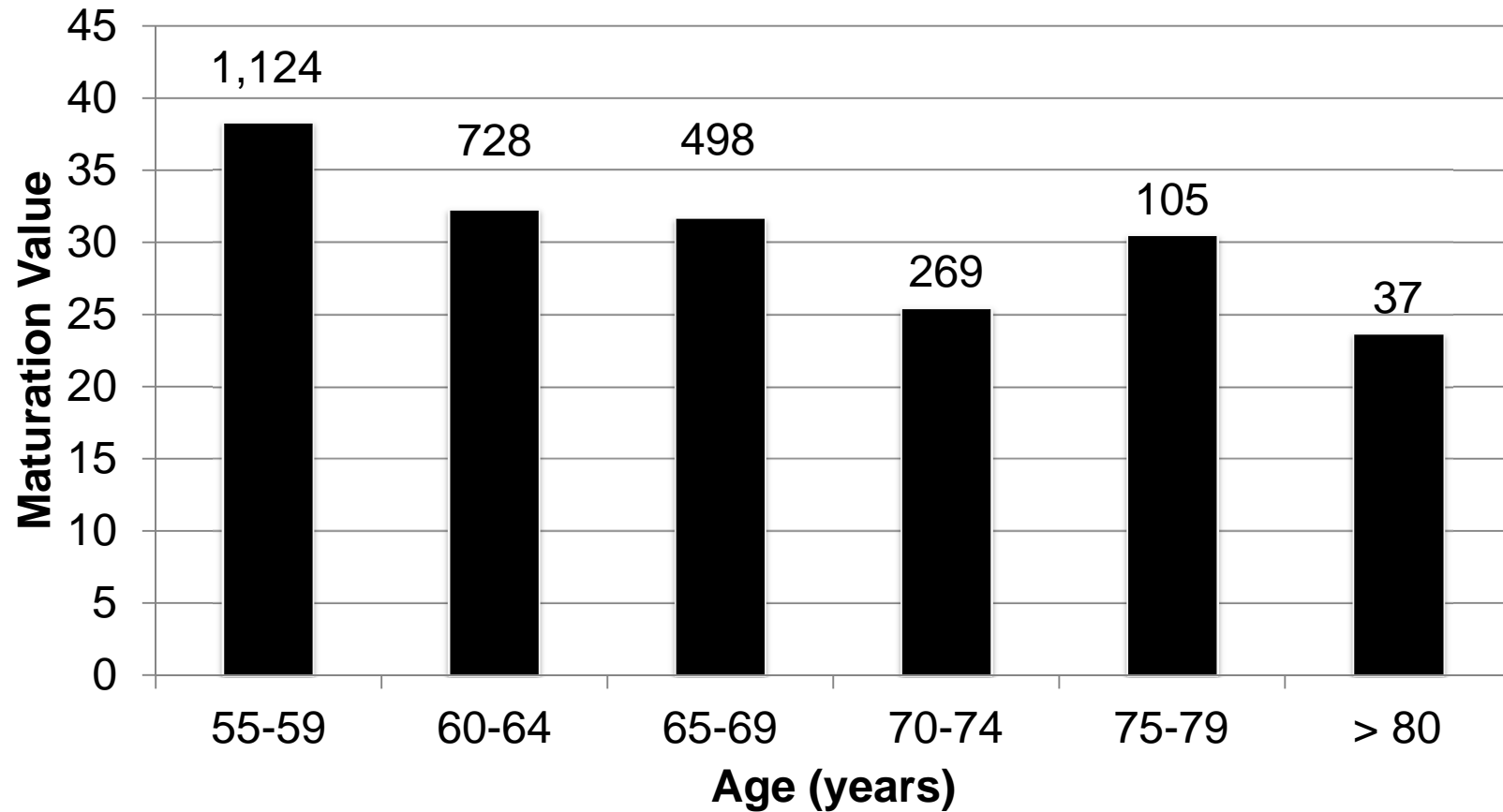
- Inversely associated with age and years since menopause  
Rationale: Results from historical clinical study (Meisels, 1966)
- Positively associated with obesity  
Rationale: Abdominal fat tissue can produce estrone
- Higher in African American women compared to other racial and ethnic groups. Rationale: Existing publications (McTernan, Wu, 2008; Setiawan, et al., 2006) and our own results from the NSHAP study suggest that African-American women have higher levels of free estradiol
- Positively associated with sexual function





# Clinical Benchmark Study of Canadian Gynecology Patients

## Meisels, 1966



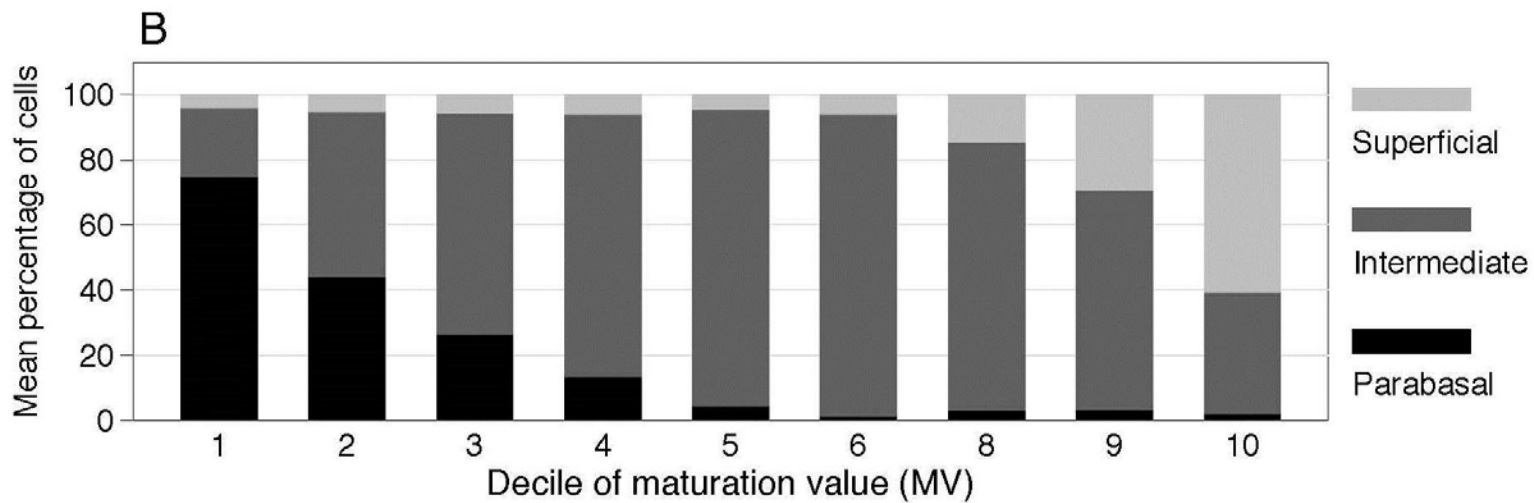
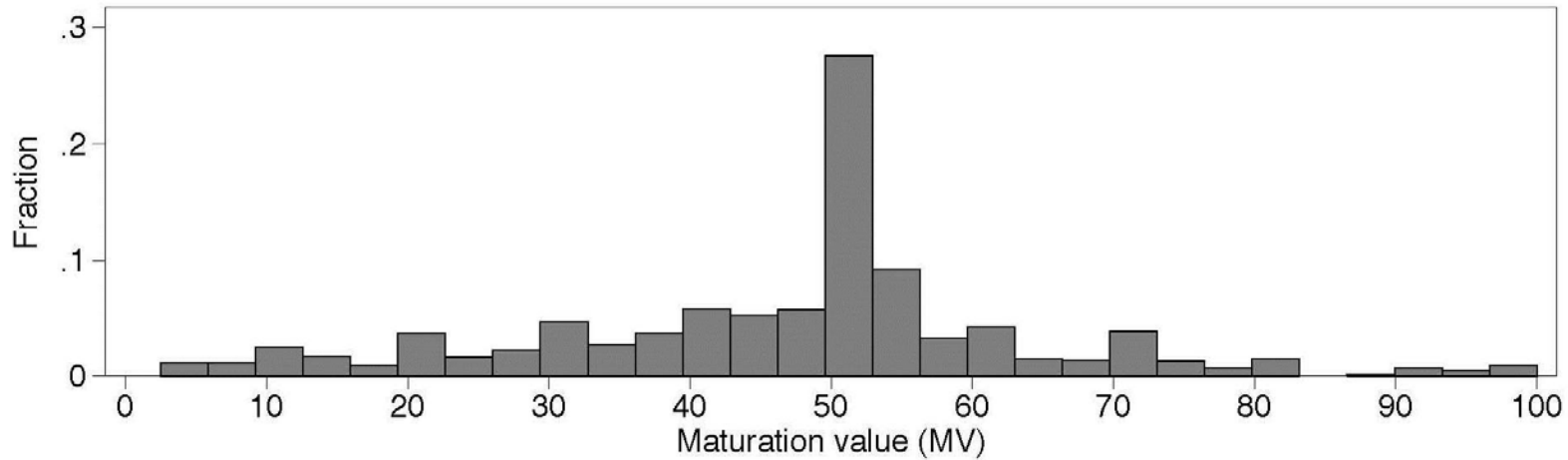
Reference: Meisels A. Menopause - A cytohormonal study. Acta Cytol. 1966;10(1):49-55



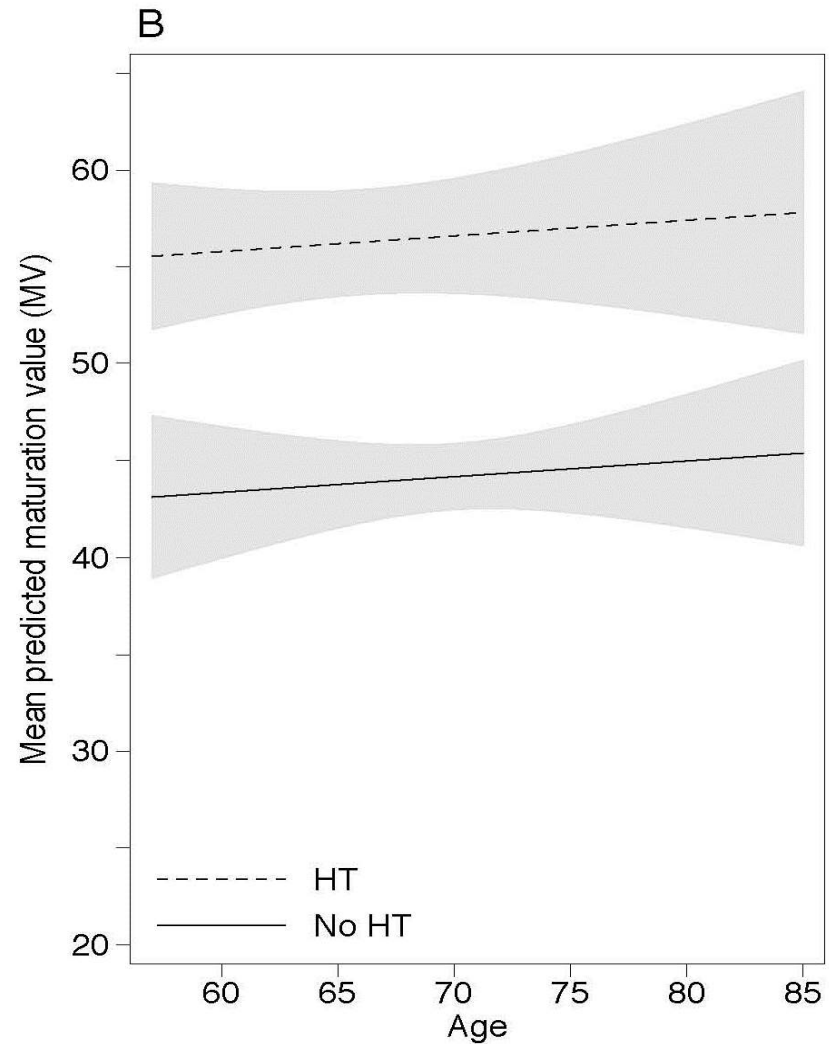
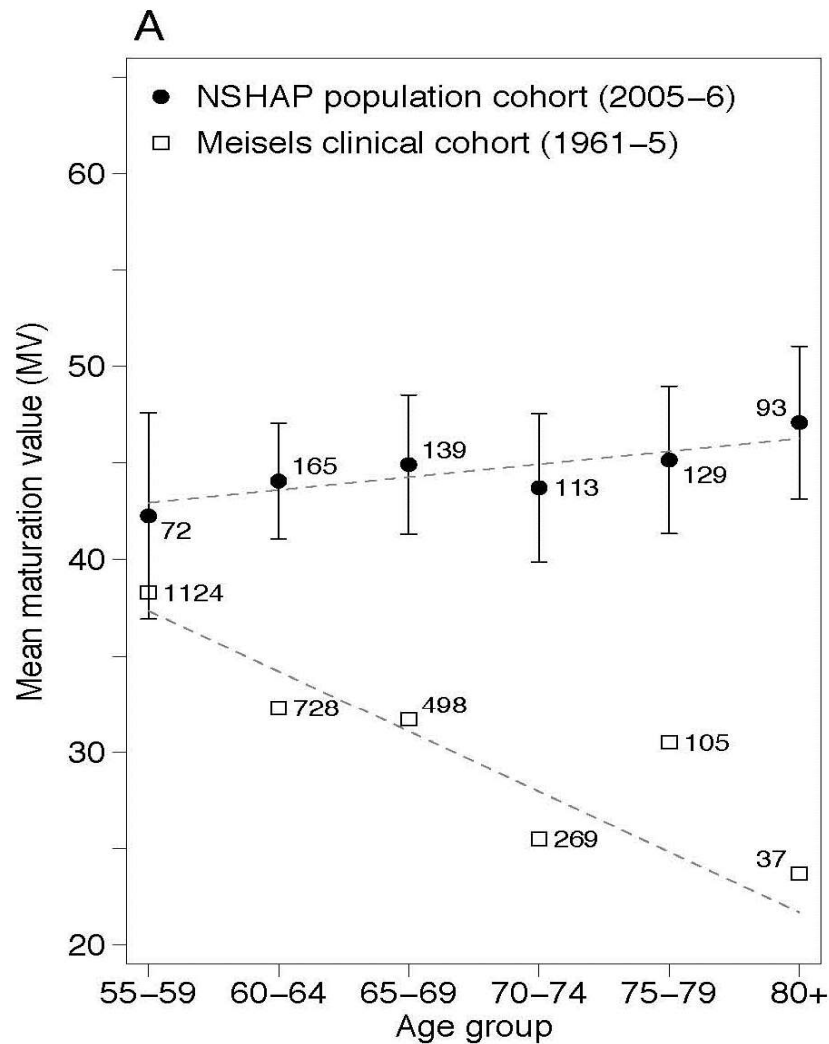
# Results



# Distribution of Maturation Value in NSHAP Wave 1



# Maturation Value: (A) Age and (B) Hormone Therapy Use



# Testing hypotheses using the maturation value

#1: Linear regression model to determine correlates (X) of the maturation value (Y).

$$Y = \beta_0 + \beta_1 X_1 + \dots + \beta_k X_k$$

$$\text{Maturation value} = \beta_0 + \beta_1 \text{hormone therapy} + \dots + \beta_k X_k$$

## Other covariates tested

### Demographic characteristics:

Age, Race, Ethnicity, Education

### Health characteristics:

Oophorectomy, Obesity, Hormone therapy past 12 mo, Sexual activity



## Multiple linear regression model of the maturation value (MV), NSHAP Wave 1

Covariate	Parameter estimate	95% CI	P-value
Age	0.08	-0.21, 0.38	0.59
Years since last menstrual period	0.10	-0.05, 0.24	0.19
African-American race (vs white, ref.)	8.58	5.07, 12.08	<0.001
Some college/associates education (vs HS graduate, ref.)	-2.64	-5.25, -0.02	0.048
HT use in last 12 months	12.44	9.19, 15.70	<0.001
Waist circumference (inches)	0.58	0.34, 0.82	<0.001

Effects of other covariates in the model (Bilateral oophorectomy, Sexual activity past 12 months and Hispanic ethnicity) turned out to be non-significant.



#2: Logistic regression using the standardized maturation value as an independent variable (X) to predict symptoms/conditions (Y).

$$\text{Prob.}(\text{symptom}) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 \text{maturation\_value} + \beta_2 \text{age} + \beta_3 \text{HT})}}$$

**Symptoms/Conditions examined:**

Sexual Activity

Pain during sex

Vaginal dryness during sex

Urinary incontinence

Bacterial vaginosis,

Yeast infection

High-risk HPV

Other urinary problems,

# Logistic regression models of clinical and behavioral outcomes on standardized maturation value (MV), NSHAP Wave 1

Outcome	Odds ratio	95% CI	P-value
Sexual activity (within the past 12 months)	0.88	0.73, 1.05	0.15
Pain during sex (for sexually active women)	0.80	0.55, 1.17	0.24
Problems lubricating (for sexually active women)	0.61	0.46, 0.82	0.001
Current bacterial vaginosis	1.54	1.26, 1.88	<0.001
Current yeast infection	1.56	1.15, 2.13	0.005
High-risk HPV	1.08	0.78, 1.51	0.63

Maturation value standardized by subtracting the sample mean and dividing by the sample standard deviation.



# Conclusions



# Hypotheses tested

Vaginal epithelial estrogenization among post-menopausal women will be:

- Inversely associated with age and years since menopause? **No**
- Positively associated with abdominal obesity: **Yes**
- Higher in African American women compared to other racial and ethnic groups: **Yes**
- Positively associated with sexual function: **Yes, mostly**



# Summary:

- Maturation value is an integrative biomeasure of estrogenization of women, useful for analyses of health and sexuality
- In contrast to 1960s benchmark clinical data, current population estimates of vaginal estrogenization are higher and do not exhibit a decline with age.
- Differences may be explained in part by studying different populations:
  - Women who come to a clinic
  - Representative sample of community-dwelling older women in the US.



# Study limitations

Selection bias: women who provided a vaginal specimen were, on average:

- younger
- more educated
- more likely to have urinary problems
- more likely to use HT





# Acknowledgements

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**Additional information can be  
found at the CCBAR website**

**<http://biomarkers.uchicago.edu/>**





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