

Cervical mucus patterns and the fertile window in women without known subfertility: A pooled analysis of 3 cohorts

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Shahpar Najmabadi, PhD, MPH, MS
Karen C. Schliep, PhD, MSPH
Sara E. Simonsen, PhD, MSPH, CNM
Christina A. Porucznik, PhD, MSPH
Marlene J. Egger, PhD
Joseph B. Stanford, MD, MSPH



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The University of Utah
Department of Family & Preventive Medicine
Office of Cooperative Reproductive Health

Introduction

- **Cervical mucus**

- A viscous fluid produced by the secretory cells of the cervical crypt
- A crucial element for the identification of ovulation (1)
- Response to highly coordinated series of hormonal fluctuations occurring within menstrual cycles (2)
- Undergoes cyclic modifications throughout the cycle
 - ❖ different biochemical and,
 - ❖ different biophysical characteristics (1) (**observable by women**)

Objectives

- To describe cervical mucus patterns and fertile window in women without known subfertility
 - Days of peak-type mucus
 - Days of non peak-type mucus
 - Total days of mucus
 - Dry days
 - Number of mucus peak days
 - Cervical mucus cycle score
 - Fertile days
 - Non fertile days
- To assess variability between women and within woman, in relation to age and parity

Source cohorts, women, and cycles

Study	Year	# Women	# Cycles	Median Cycles per Woman	Range
CEIBA	2009–2013	232	1,257	5	1–15
TTP	2003–2006	46	136	3	1–7
CMFS	1990–1996	168	763	6	1–14
Total		446	2,156	5	1–15

CEIBA: Creighton Model Effectiveness, Intentions, and Behaviors Assessment

TTP: Time to Pregnancy in Normal Fertility

CMFS: Creighton Model MultiCenter Fecundability Study

Stanford JB, Porucznik CA. *Frontiers in Medicine (Lausanne)*. 2017;4:147.

Stanford JB, Smith KR, Varner MW. *Paediatric Perinatal Epidemiology*. 2014;28(5):391-9.

Stanford JB, Smith KR, Dunson DB. *Obstetrics Gynecology*. 2003;101(6):1285-93.



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Selection criteria

- New users of the **Creighton Model FertilityCare System**
- Age 18-40
- History of regular cycles
- No history of subfertility, endometriosis, PCOS, thyroid disease.
- Exclude women who had discontinued oral contraceptives within past 60 days.
- Ovulatory cycles only (mucus peak day).
- Exclude cycles with drugs that would affect ovulation or mucus.

Methods

Stamp	Date	Description
	4/10	VL M OAD?
	4/11	N/H
	4/12	N/L
	4/13	N/L
	4/14	L/V
	4/15	VL OAD
	4/16	10 c/k BSE
	4/17	11 c/k x1 yes
	4/18	12 c/k x1 no yes
	4/19	13 c/k x1 no ↑
	4/20	14 c/k x1 yes
	4/21	15 c/k x1 yes
	4/22	16 c/k x1 yes
	4/23	17 c/k x2 yes
	4/24	18 c/k x1 yes
	4/25	19 c/k x1 yes
	4/26	20 c/k x1 no
	4/27	21 c/k x1 yes
	4/28	22 c/k x2 yes
	4/29	23 c/k x2 yes
	4/30	24 c/k x2 AD
	5/1	25 c/k x2 yes
	5/2	26 c/k x2 yes
	5/3	27 c/k x2 yes
	5/4	28 c/k x2 AD
	5/5	29 c/k x2 AD
	5/6	30 c/k x2 AD
	5/7	31 c/k x2 AD
	5/8	1 AD
	5/9	2 AD
	5/10	3 AD
	5/11	4 AD
	5/12	5 AD
	5/13	6 AD
	5/14	7 AD

- Woman recorded vaginal bleeding or discharge daily
- Creighton Model Chart (CrM)
- Last day of discharge that is clear, stretchy or slippery
 - Peak day = estimated day of ovulation
 - True peak confirmed by two reviewers

Statistical Analysis

- Secondary data analysis
 - Descriptive
- Repeated measures (longitudinal data)
- Generalized Linear Mixed Models
 - Least square mean
 - Risk Ratio
 - Woman level variability
- SAS software (9.4 – North Carolina)



Results

Between Women



Demographic Information (n=446)

- Mean age 27.2 ± 4.2 years (Range 18–40)
- 87% non-Hispanic white
- 89% married or engaged
- 76% college graduates
- 77% employed
- 23 locations in USA, one in Canada

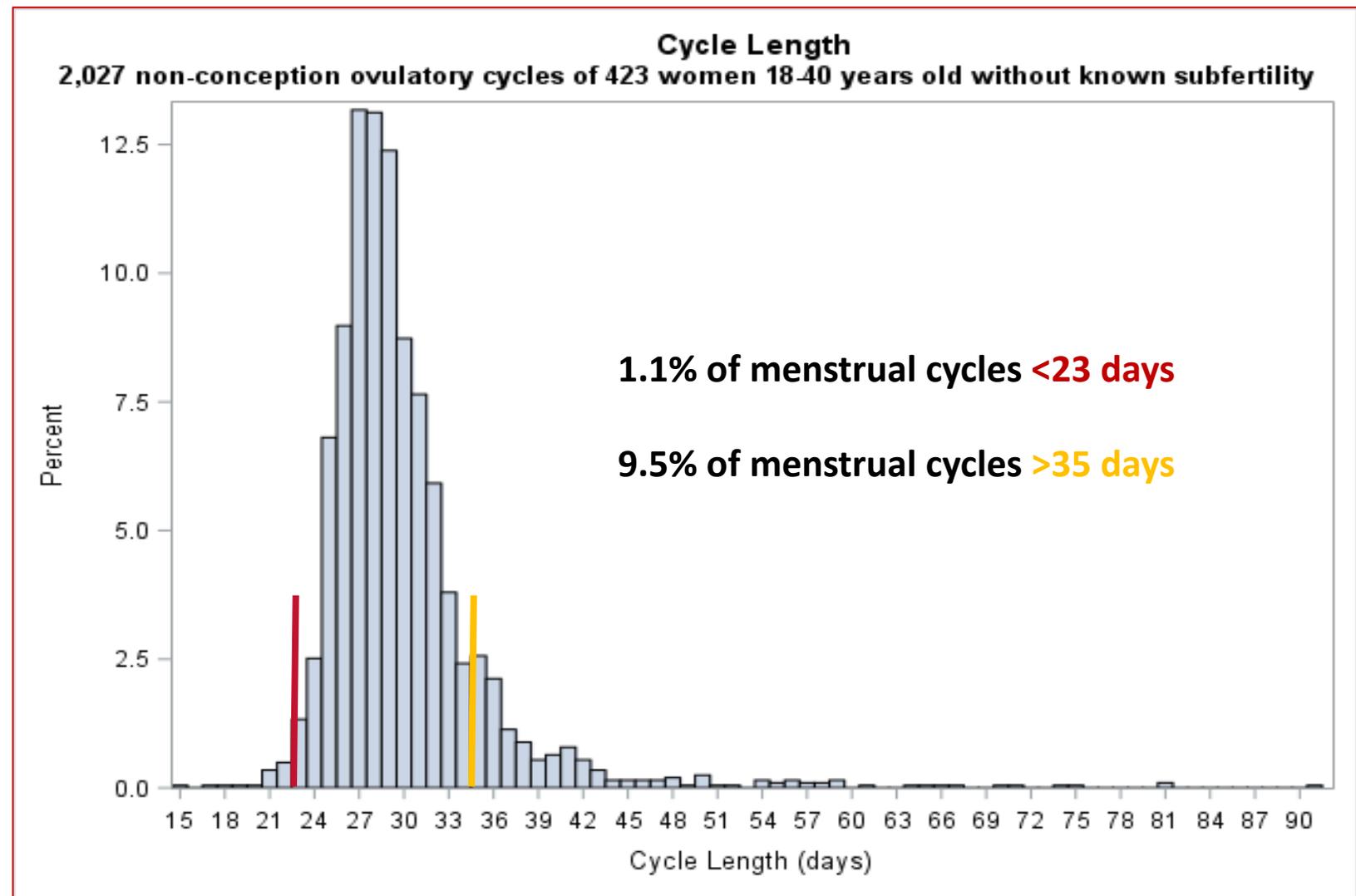


Reproductive History (n=446)

- 83% menarche between 11–14 years old
- 66% nulligravid
- 71% nulliparous



Cycle Length

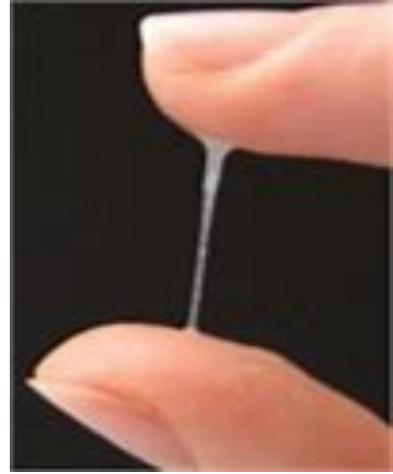


Characteristics	Mean ± STD	Median	IQR	Range
Cycle length (day)	29.9 ± 5.9	29	27–31	15–91

Ovulation

- By design, 100% of cycles (2,156) had a mucus peak day (estimated day of ovulation) and were used for analysis of cycle phase lengths.
- Follicular phase included estimated day of ovulation.

Mucus Type



Days of peak-type mucus

Any mucus discharge that is clear, stretchy (an inch or more), and/or lubricative

Days of non peak-type mucus

Any other mucus

Dry days

Days without any mucus observation (includes damp or shiny alone)

Number of peak days

Any mucus peak requiring a count of three following (including 3 or more days of nonpeak mucus)



Mucus days **within follicular phase**

2,152 cycles, 444 women

Characteristics	Mean \pm STD	Median	IQR	Range
Days of peak-type mucus	5.7 \pm 3.3	5	4–7	0–33
Days of non peak-type mucus	2.6 \pm 3.0	2	0–4	0–49
Total days of mucus	8.3 \pm 4.6	8	5–10.5	1–55
Dry days	9.2 \pm 4.9	9	6–11	1–55

Mucus status **within follicular phase**, by Parity and Age

	<u>Nulliparous</u>		<u>Parous</u>	
	Age <30	Age ≥ 30	Age <30	Age ≥ 30
Days of peak-type mucus	5.7 (5.3, 6.0)	5.0 (4.2, 5.7)	6.6 (5.9, 7.3)	6.0 (5.3, 6.8)
Days of non peak-type mucus	2.8 (2.4, 3.1)	2.0 (1.3, 2.7)	2.0 (1.3, 2.7)	2.9 (2.1, 3.7)
Total days of mucus	8.4 (7.9, 9.0)	7.0 (5.8, 8.1)	8.6 (7.6, 9.6)	8.9 (7.8, 10.0)
Dry days	10.0 (9.5, 10.5)	9.4 (8.3, 10.5)	8.3 (7.4, 9.2)	8.5 (7.5, 9.5)

- Nulliparous women age ≥30 years versus <30 had significantly fewer days of non peak-type mucus and fewer total days of mucus.

Mucus status **in full cycle**, by Parity and Age

2,027 **non conception** cycles mean (95% CI) of 423 women

	<u>Nulliparous</u>		<u>Parous</u>	
	Age <30	Age ≥ 30	Age <30	Age ≥ 30
Days of peak-type mucus	6.4 (5.9, 6.8)	5.5 (4.6, 6.4)	8.0 (7.0, 9.1)	6.9 (5.7, 8.0)
Days of non peak-type mucus	5.4 (4.8, 6.0)	3.9 (2.7, 5.1)	4.9 (3.6, 6.2)	6.3 (4.9, 7.8)
Total days of mucus	11.7 (10.9, 12.5)	9.4 (7.7, 11.1)	12.9 (11.2, 14.6)	13.2 (11.3, 15.1)
Dry days	18.5 (17.7, 19.4)	18.9 (17.2, 20.6)	15.6 (13.9, 17.2)	15.8 (14.0, 17.6)

- Nulliparous women age ≥30 years versus <30 had significantly fewer days of non peak-type mucus and fewer total days of mucus.

Number of mucus peak days **in full cycle** by Parity and Age

2,027 **non conception** cycles mean (95% CI) of 423 women

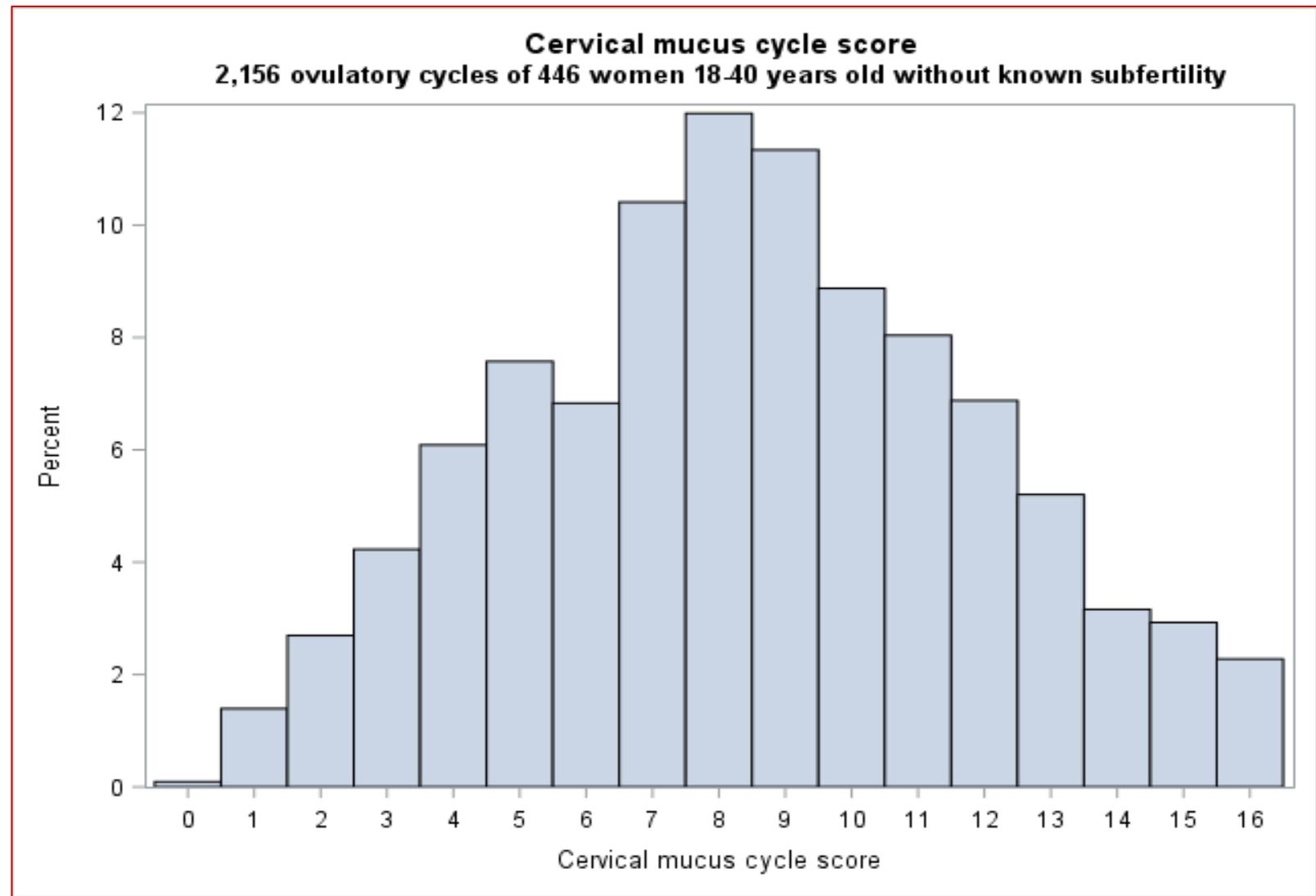
Characteristics	Mean \pm STD	Median	IQR	Range
Number of mucus peak days	1.8 \pm 1.1	2	1–2	1–10

	<u>Nulliparous</u>		<u>Parous</u>	
	Age <30	Age \geq 30	Age <30	Age \geq 30
Number of mucus peak days	1.9 (1.8, 2.0)	1.8 (1.5, 2.0)	1.9 (1.7, 2.2)	1.8 (1.6, 2.1)

Cervical Mucus Cycle Score

- To assess the quality of mucus objectively
- Point values assigned to 4 major components of vulvar mucus observations
 - consistency
 - sensation
 - color
 - change
- Points tallied for the six days of the mucus cycle or estimated **fertile window**
 - beginning five days prior to the peak day and including the peak day
- As fertility increases, the total score gets closer to the highest total of 16.
- Developed by TW Hilgers

Cervical mucus cycle score



Characteristics	Mean \pm STD	Median	IQR	Range
Mucus cycle score	8.4 \pm 3.5	8.3	6–11	0–16

Cervical mucus cycle score by Parity and Age

	<u>Nulliparous</u>		<u>Parous</u>	
	Age <30	Age ≥ 30	Age <30	Age ≥ 30
Cervical mucus cycle score	8.2 (7.8, 8.5)	7.8 (7.0, 8.6)	9.4 (8.7, 10.0)	8.8 (8.0, 9.5)



Fertile days

- Days with a significant probability of pregnancy if intercourse were to occur on that day
- Most days with mucus except
 - unchanging mucus patterns
 - or mucus days that occur more than 3 days after true peak
- Three days following any peak day
- Days of abnormal spotting

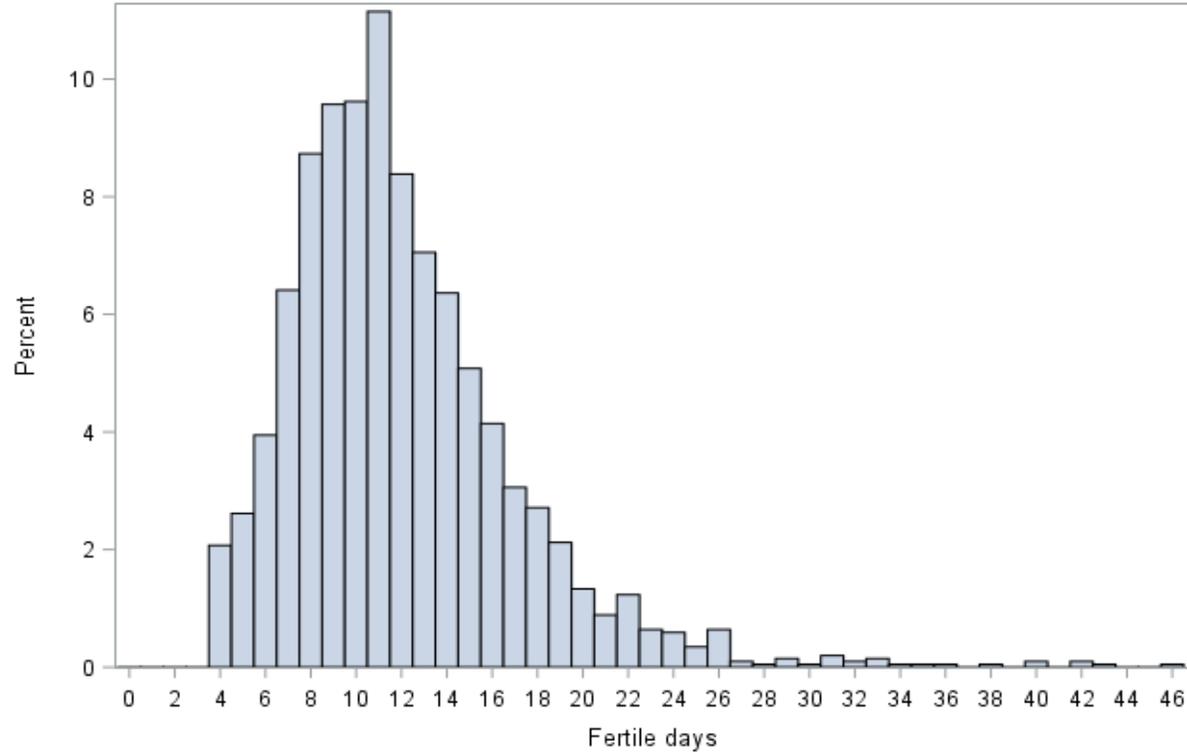
Non-fertile days

- Days with a minimal probability of pregnancy if intercourse were to occur on that day
- All dry days except
 - those that occur within 3 days following a peak day
 - or that have spotting
- Heavy or moderate bleeding days in menstrual flow

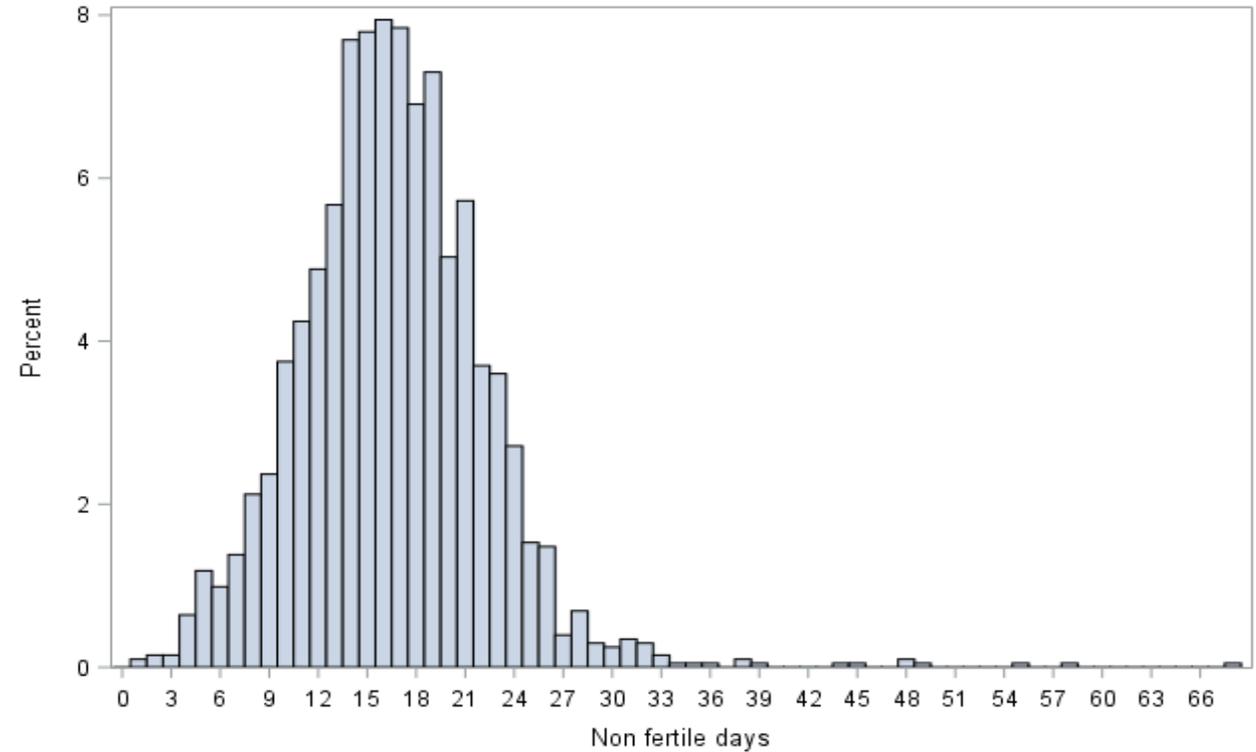


Fertile and Non fertile Days, full cycle

Fertile days
2,027 non-conception ovulatory cycles of 423 women 18-40 years old without known subfertility



Non fertile days
2,027 non-conception ovulatory cycles of 423 women 18-40 years old without known subfertility



Characteristics

Mean \pm STD

Median

IQR

Range

Fertile days

12.0 \pm 5.0

11

9–14

4–46

Non fertile days

16.6 \pm 5.8

16

13–20

1–68

Days of Unknown fertility

1.4 \pm 1.9

1

0–2

0–21

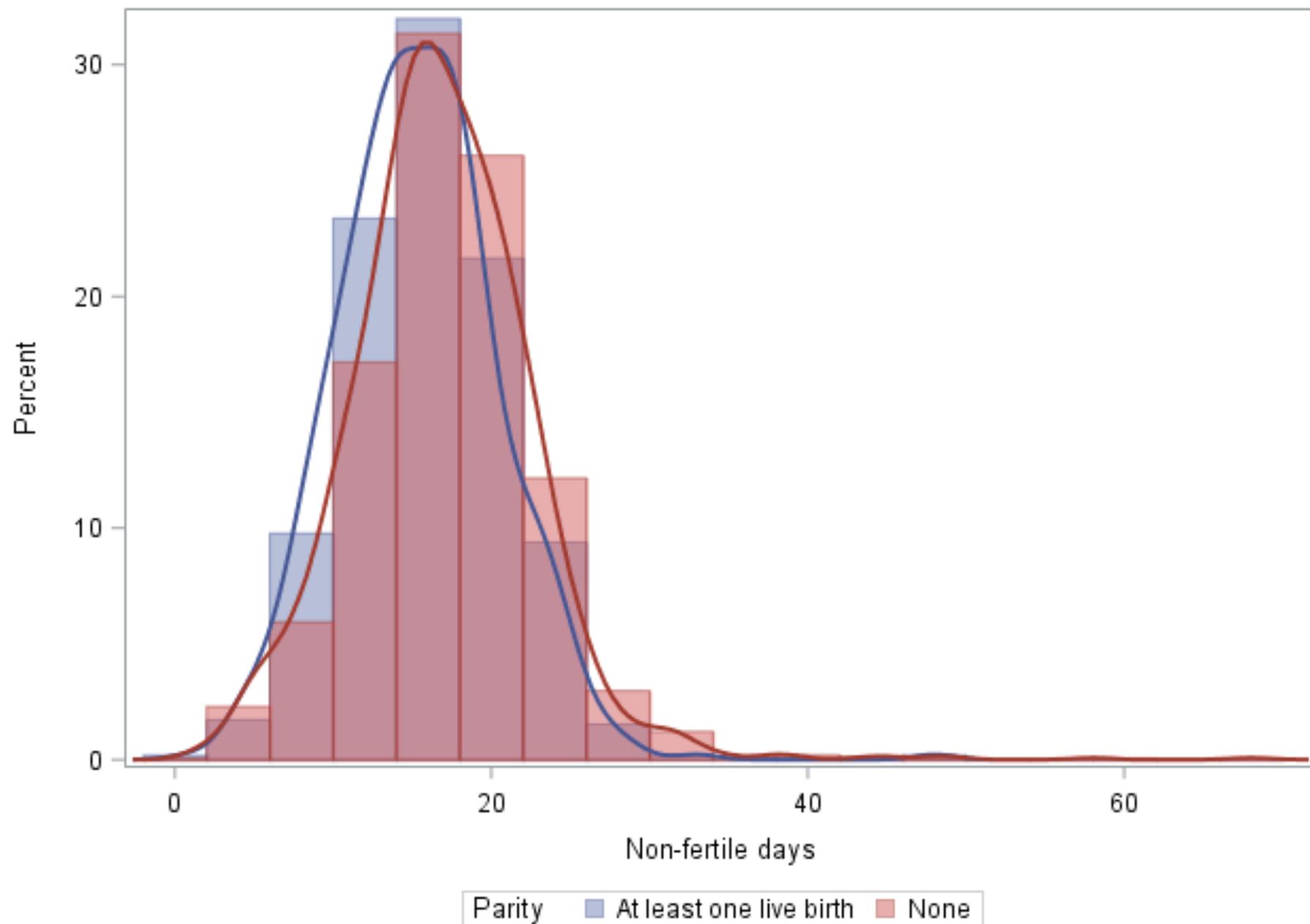
Fertility status, by Parity and Age

2,027 **non conception** cycles mean (95% CI) of 423 women

	<u>Nulliparous</u>		<u>Parous</u>	
	Age <30	Age ≥ 30	Age <30	Age ≥ 30
Fertile days	12.5 (12.0, 13.0)	10.6 (9.5, 11.7)	13.0 (11.9, 14.2)	12.9 (11.6, 14.1)
Non fertile days	17.1 (16.5, 17.7)	16.9 (15.6, 18.1)	15.3 (14.1, 16.5)	15.6 (14.3, 16.9)

- Nulliparous women age ≥30 years versus <30 had significantly fewer fertile days.

Distribution of non-fertile days by Parity, $P=0.0026$



Results

Within Woman (up to 1 year)



Cervical mucus variability (within women)

- 69% most – fewest days of peak-type mucus >3 days
- 60% most – fewest days of non peak-type mucus >3 days
- 69% highest – lowest cervical mucus cycle score >4 points
- 46% most– fewest fertile days >8 days
- 59% most– fewest non fertile days >8 days
- No significant differences by age or parity

○ Strengths

- Cohort with prospectively collected daily charting
- Assess short-term variability

○ Limitations

- Possibility of unknown subfertility or gynecologic disorder
- Do not have Body Mass Index
- Limited ethnic and SES diversity
- Possible contribution of seminal fluid



Discussion

- Ovulatory cycles have a spectrum of ovulatory and hormonal function, so that ovulatory status is more accurately defined as a spectrum of function rather than a solely binary designation ⁽¹⁾
- Women's self-observed cervical mucus patterns can identify characteristics of the fertile window and reproductive function that vary somewhat with parity and age
- Substantial within-woman variability of the duration and quality of cervical mucus is likely a result of ongoing interaction between the body and external environment (Hypothalamus-Pituitary-Ovary Axis)

1. Brown JB. Human reproduction update. 2011;17(2):141-58.

Questions