



Primary care approach to infertility

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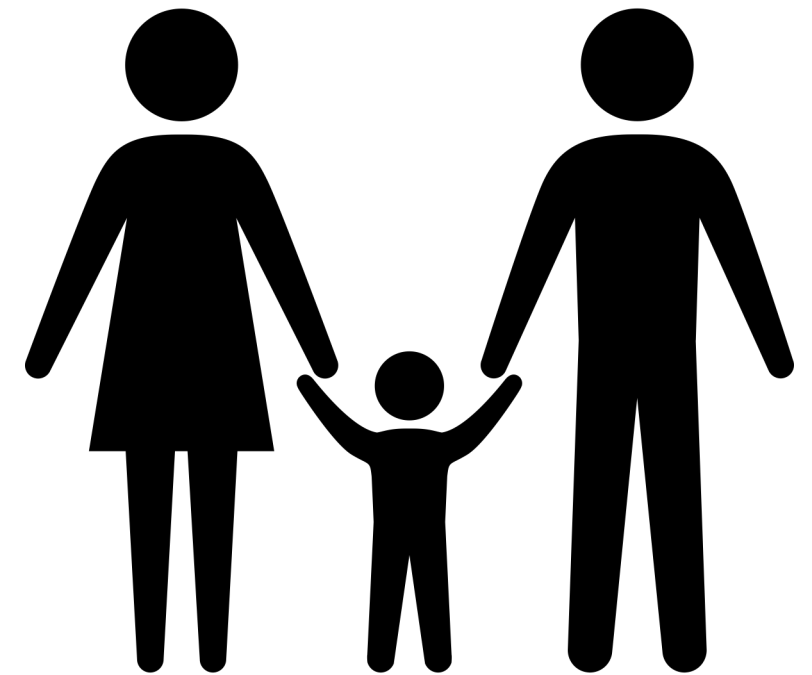
Objectives

- Describe the incidence, prevalence, and resolution of infertility in the general population.
- Outline the main underlying causes of infertility.
- Describe a primary care approach to evaluating and treating infertility.

Infertility

- Relevance
- Descriptive epidemiology
- Causes
- Primary care approach
 - Lifestyle
 - Diagnosis
 - Treatment
 - Referral

10-15% of couples report that they are unable to have the number of children that they would like to have.



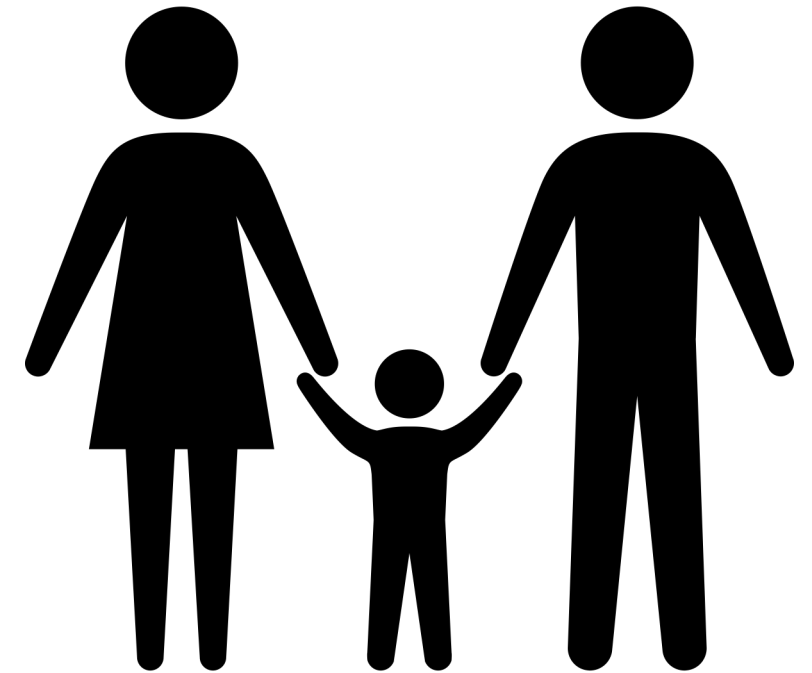
Population-based survey of **women**
age 40-55 in UK for *lifetime* infertility

16% had consulted doctor for
problems conceiving

8% had fertility treatment

2.4% never conceived

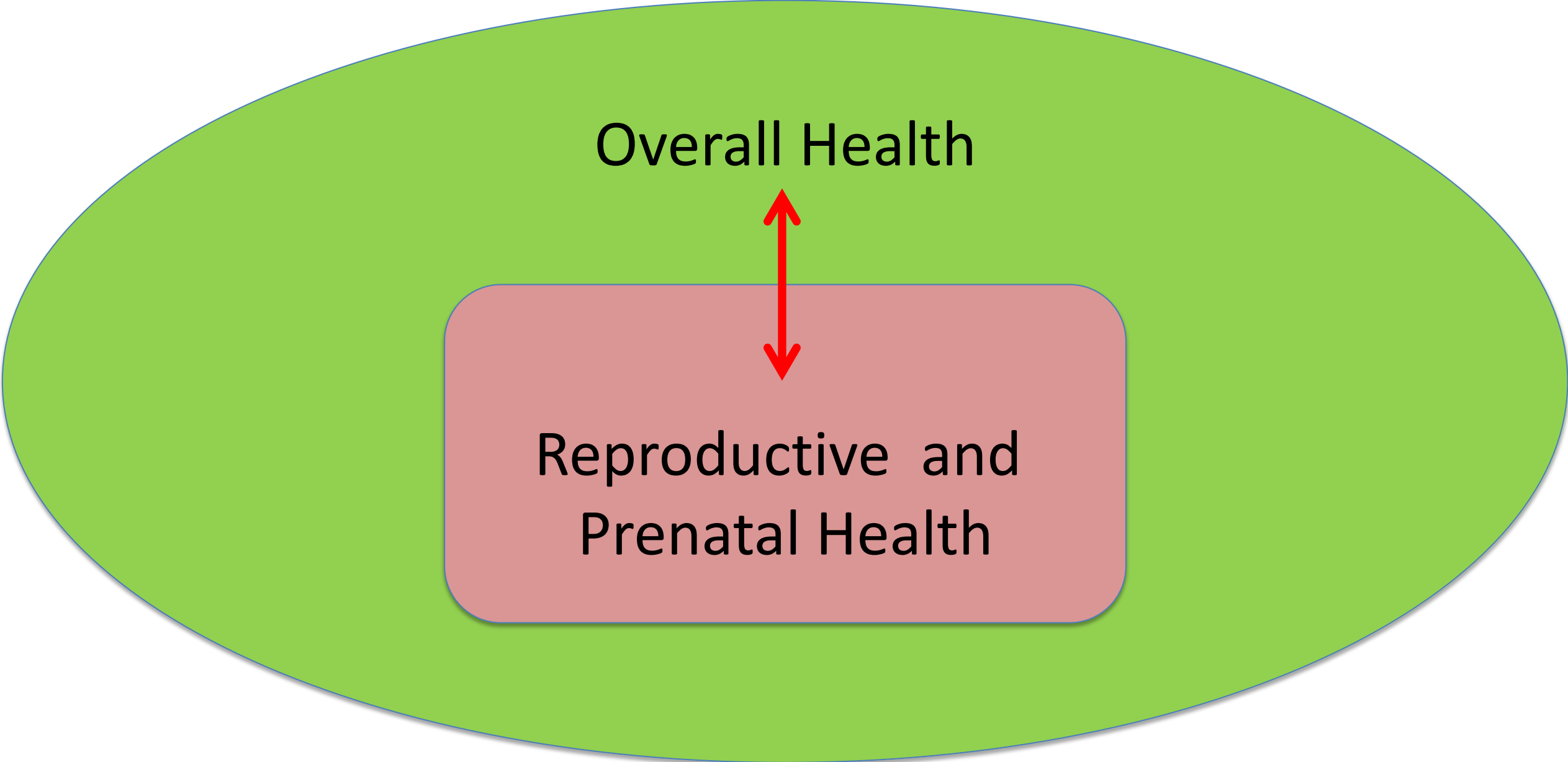
1.9% conceived but no live birth



Oakley et al. *Hum Reprod* 2008

Fertility problems are also related to

- Pregnancy loss
- Perinatal outcomes
- Other chronic conditions and health risks in women and men
- Psychological and relationship stress



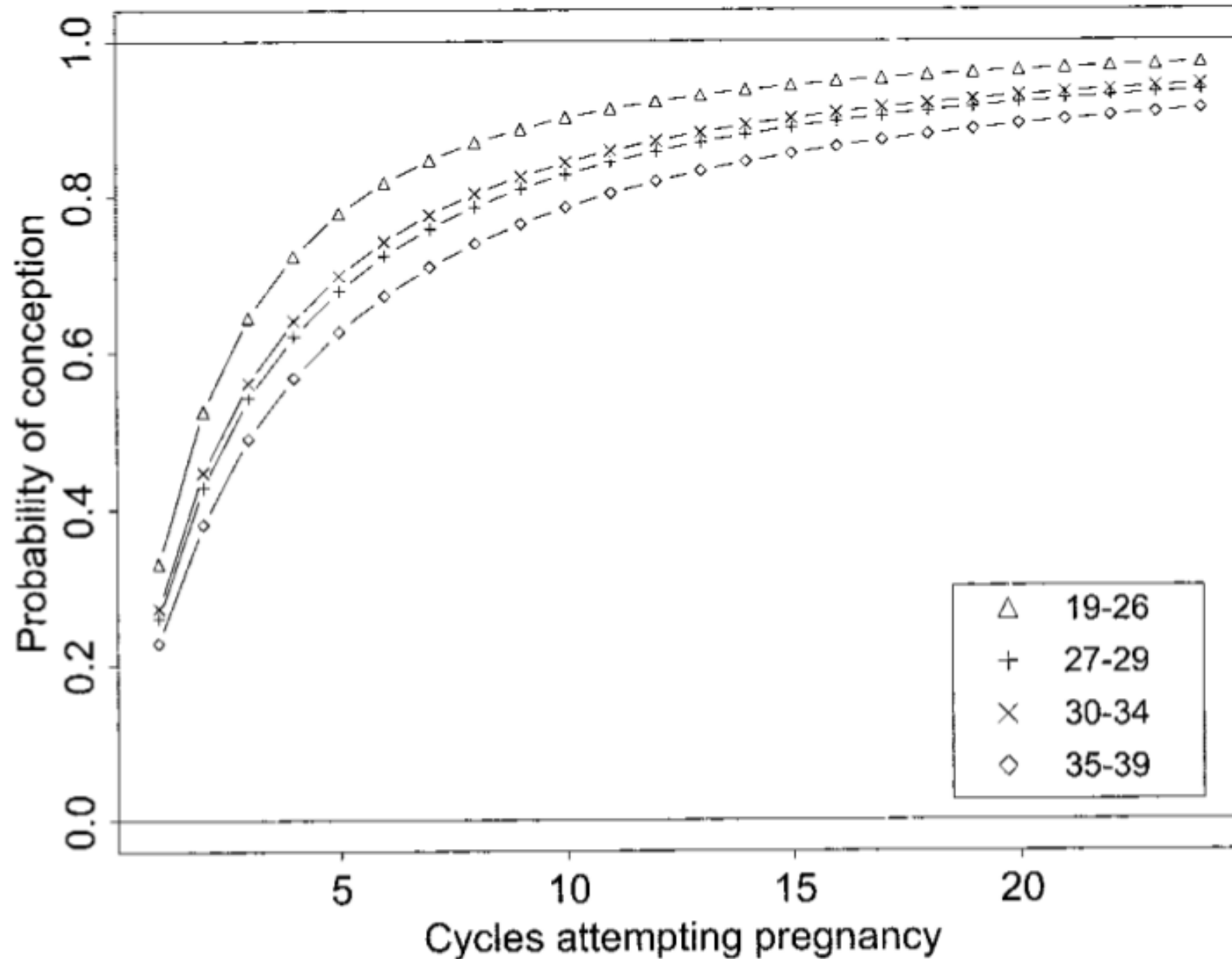
Overall Health

Reproductive and
Prenatal Health

Fertility (fecundity) is a spectrum

- Matter of probability and time
- The time cutoffs used to identify a fertility problem (usually 1 year) are by convention, not based on any biological threshold.
- It takes two (for natural conception)
- Usually not diagnosed until “trying”

Fertility (fecundity) is a spectrum



“The estimated percentage of infertile couples that would be able to conceive after an additional 12 cycles of trying varied from 43-65% depending on age.”

Dunson et al.
Obstet Gynecol 2004

What is “trying”?

- “Regular” intercourse without contraception
 - Once a week? Twice a week? More?
- Tracking your cycle and ovulation?
- Intercourse targeted to the fertile window?
- Common for couples to say: we haven’t (always) been using contraception, but we haven’t started trying yet.

Definitions

- **Primary infertility:** No prior pregnancy (or birth)
- **Secondary infertility:** Prior pregnancy (or birth)

Infertility

- Syndrome, not one disease
- Multiple underlying conditions
- One of our studies of 370 couples, in review, found a mean of 5.5 related diagnoses per couple.
- About half of couples have a male component

Clinical infertility

- $\frac{1}{2}$ of couples ever go to a doctor for advice.
- $\frac{1}{2}$ of those who go to a doctor ever get diagnostic procedures or treatment
- Variation in evaluation and treatment

Lifestyle

- Don't smoke
- Moderate alcohol and caffeine
- Exercise
- Maintain good metabolic health

Clinical vs. population-based sample (n=960)

	Clinic	Population
Ever received medical treatment	91%	59%
Ever had IVF	46%	14%
Had a subsequent live birth	55%	52%

Stanford et al. *Paed Perinat Epidemiol* 2016

Female: common underlying conditions

- Polycystic ovarian syndrome
 - Sporadic or chronic anovulation (longer cycles)
 - Facial hair via excess androgens
 - Multiple *small* cysts on ovaries, ovaries enlarged
 - Insulin resistance
 - “Ovarian metabolic syndrome”

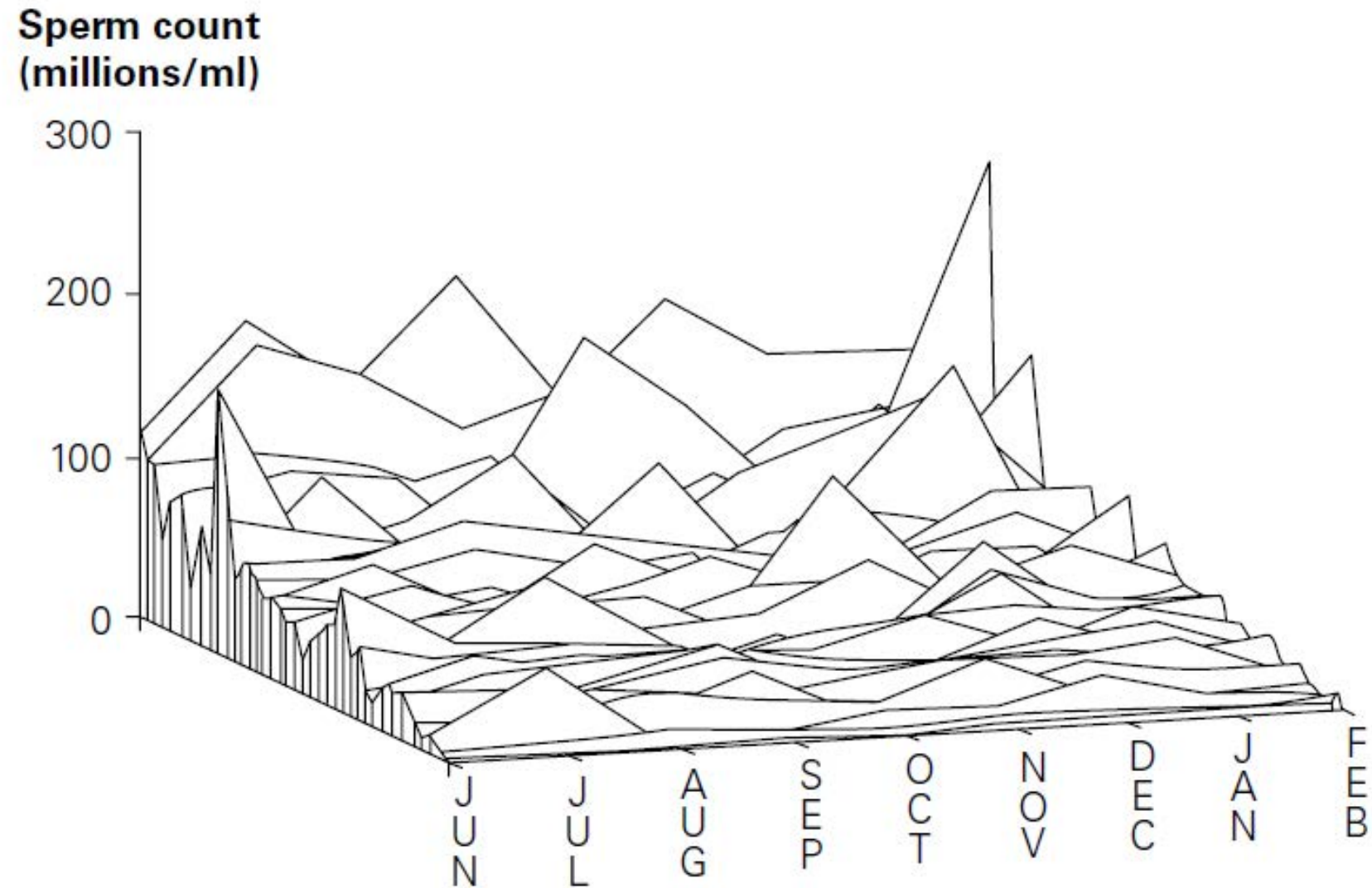
Female: common underlying conditions

- Ovulatory disorders for other reasons than PCOS
 - Obesity
 - Underweight (eating disorder, others)
 - Thyroid
- Endometriosis
- Prior pelvic infections
- Tobacco, other substances

Male underlying conditions

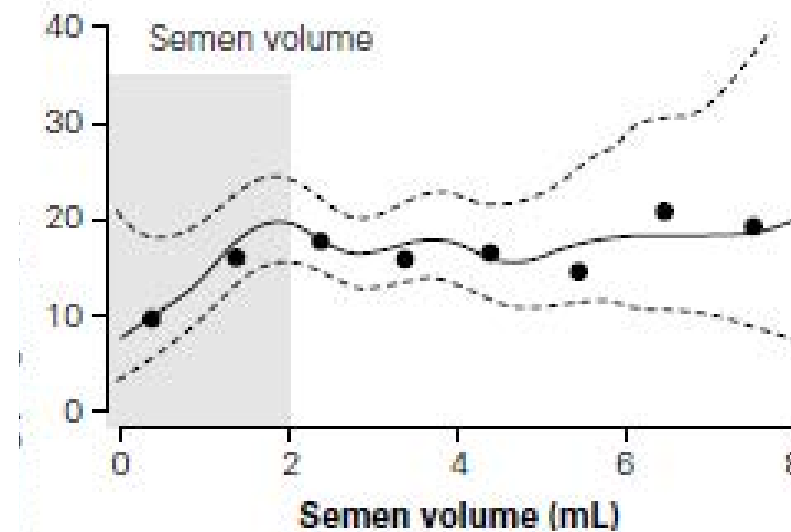
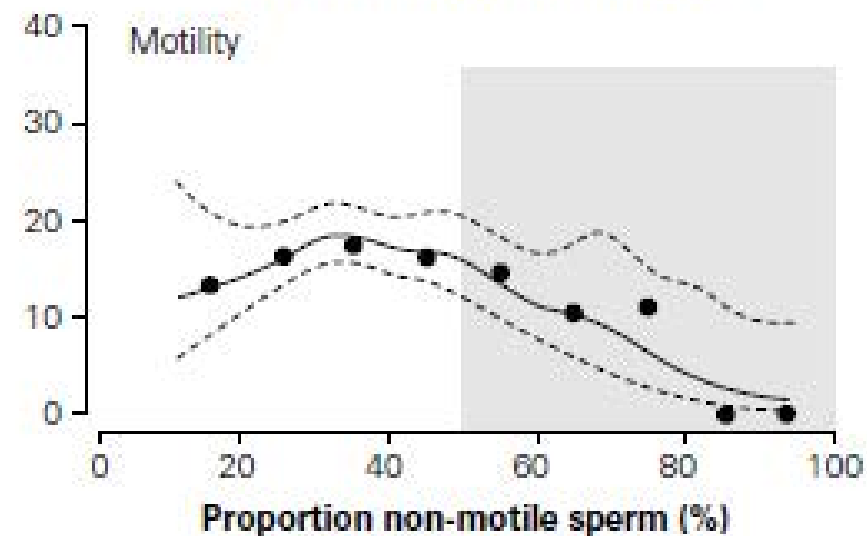
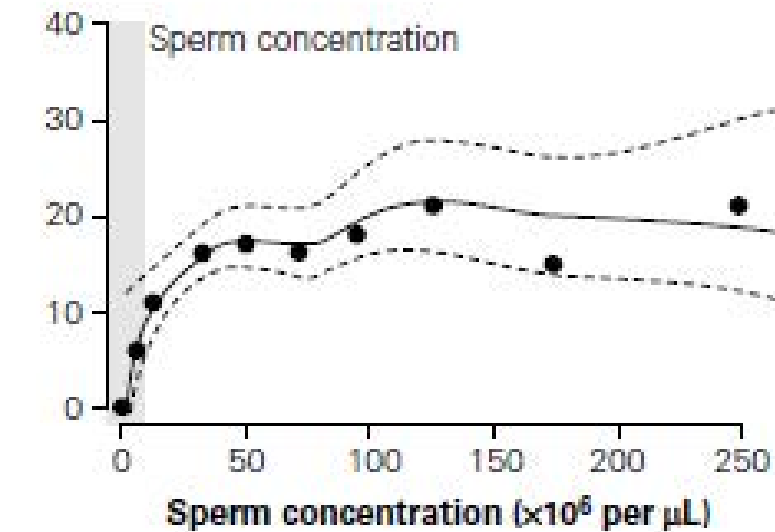
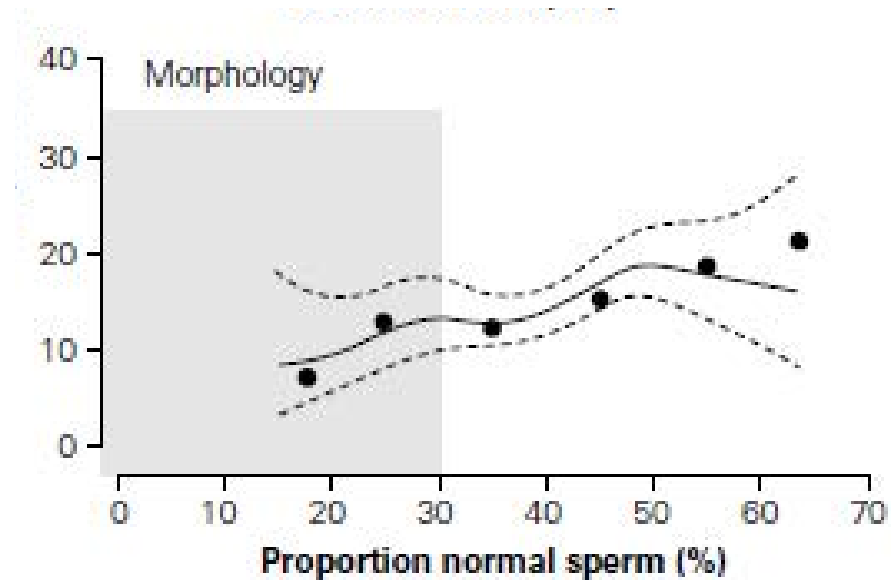
- Congenital
 - Undescended testicles
 - Microdeletions in Y chromosome
- Varicocele (varicose veins of testes)
- Obesity
- Tobacco
- Androgenic steroids!

Sperm concentrations over time (45 men, 9 months)



Wilcox, 2010

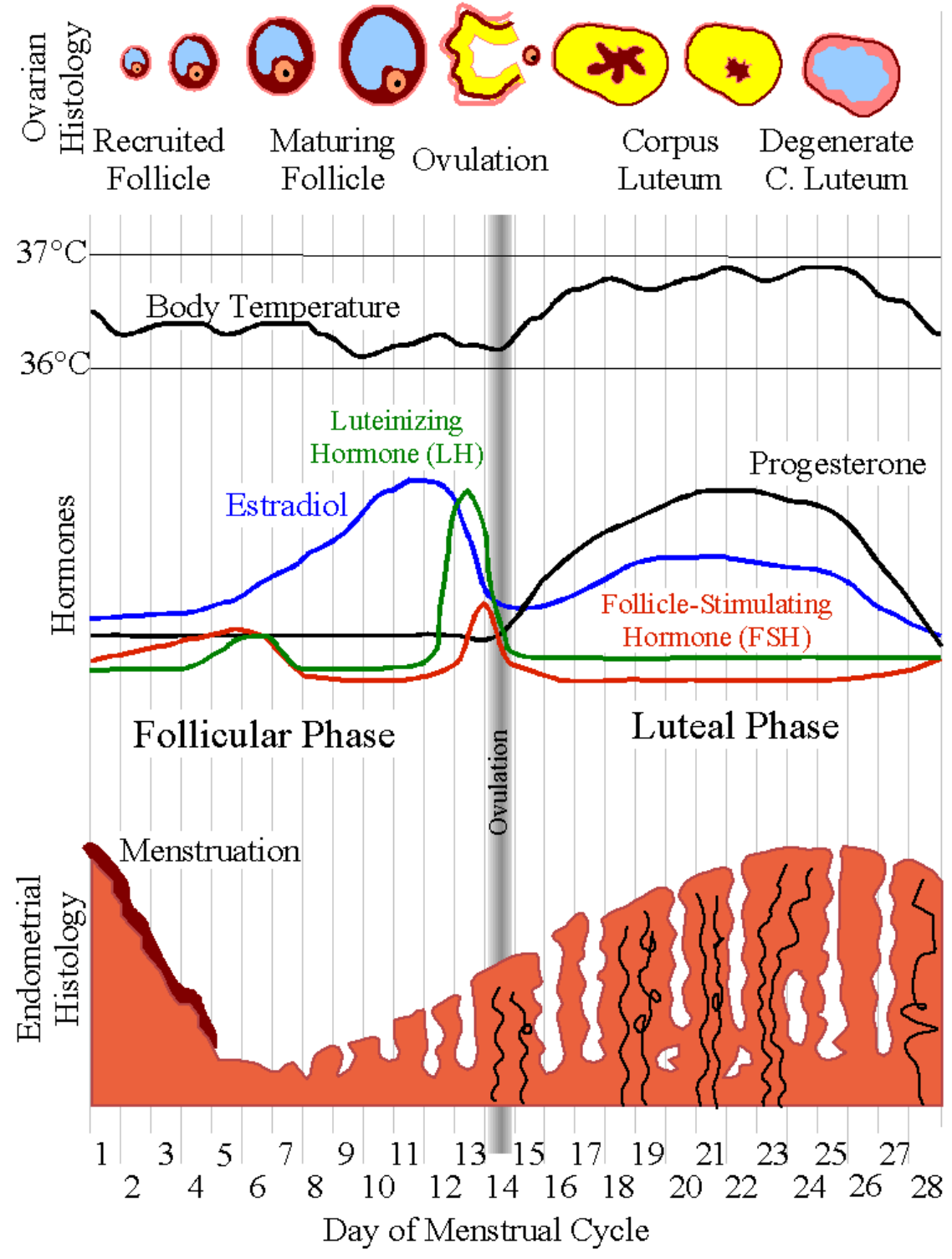
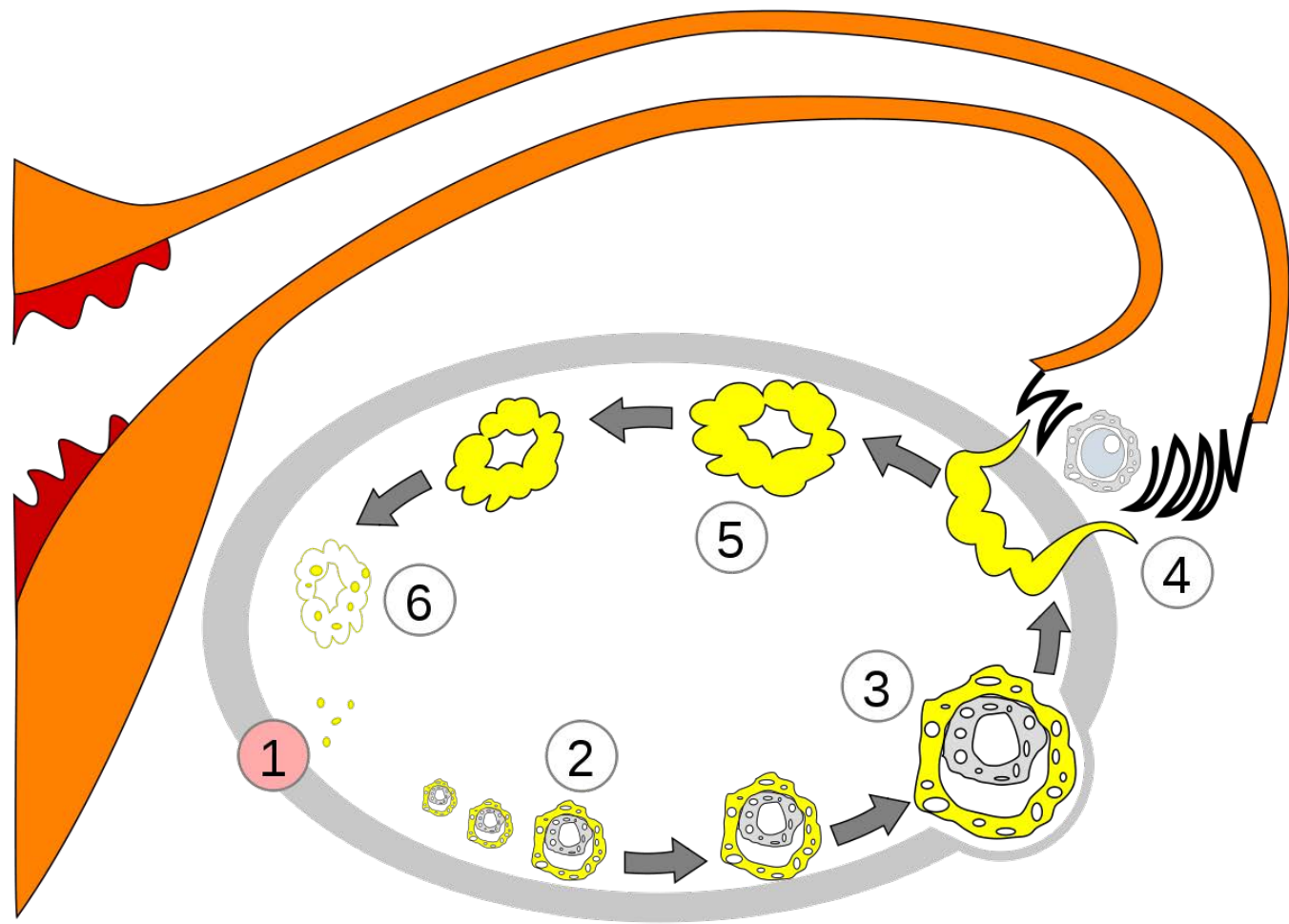
Male fecundability and semen parameters



Wilcox, from Bonde et al. 1988

Fertility awareness

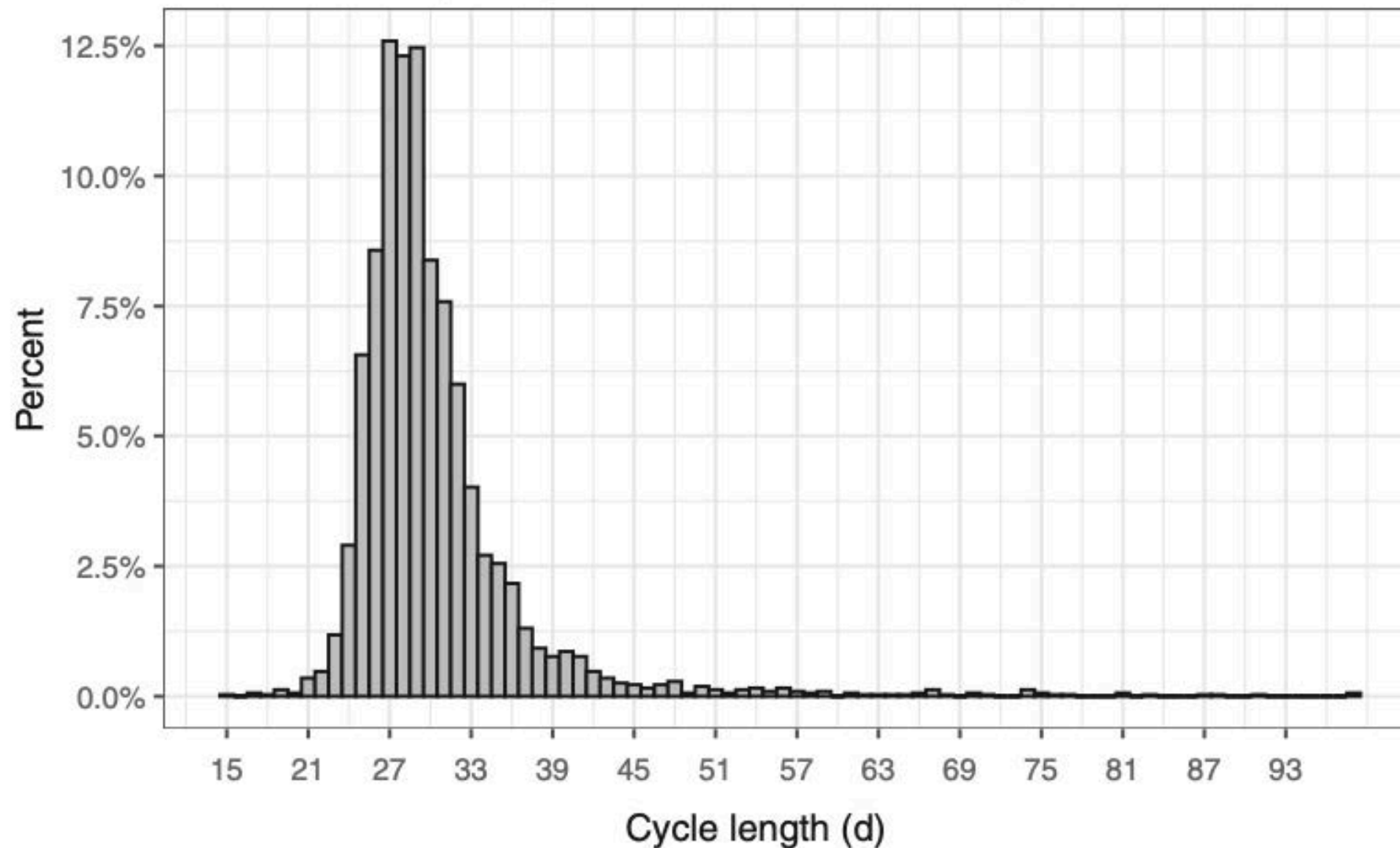
- Menstrual Cycle
 - Starts with menstrual bleeding (visible), but more important event is ovulation
- Fertile window = days of cycle when intercourse likely to result in pregnancy



The menstrual cycle: cycle length

(a) Distribution of cycle length

3137 non-conception cycles, 562 women 18- to 40-y-old



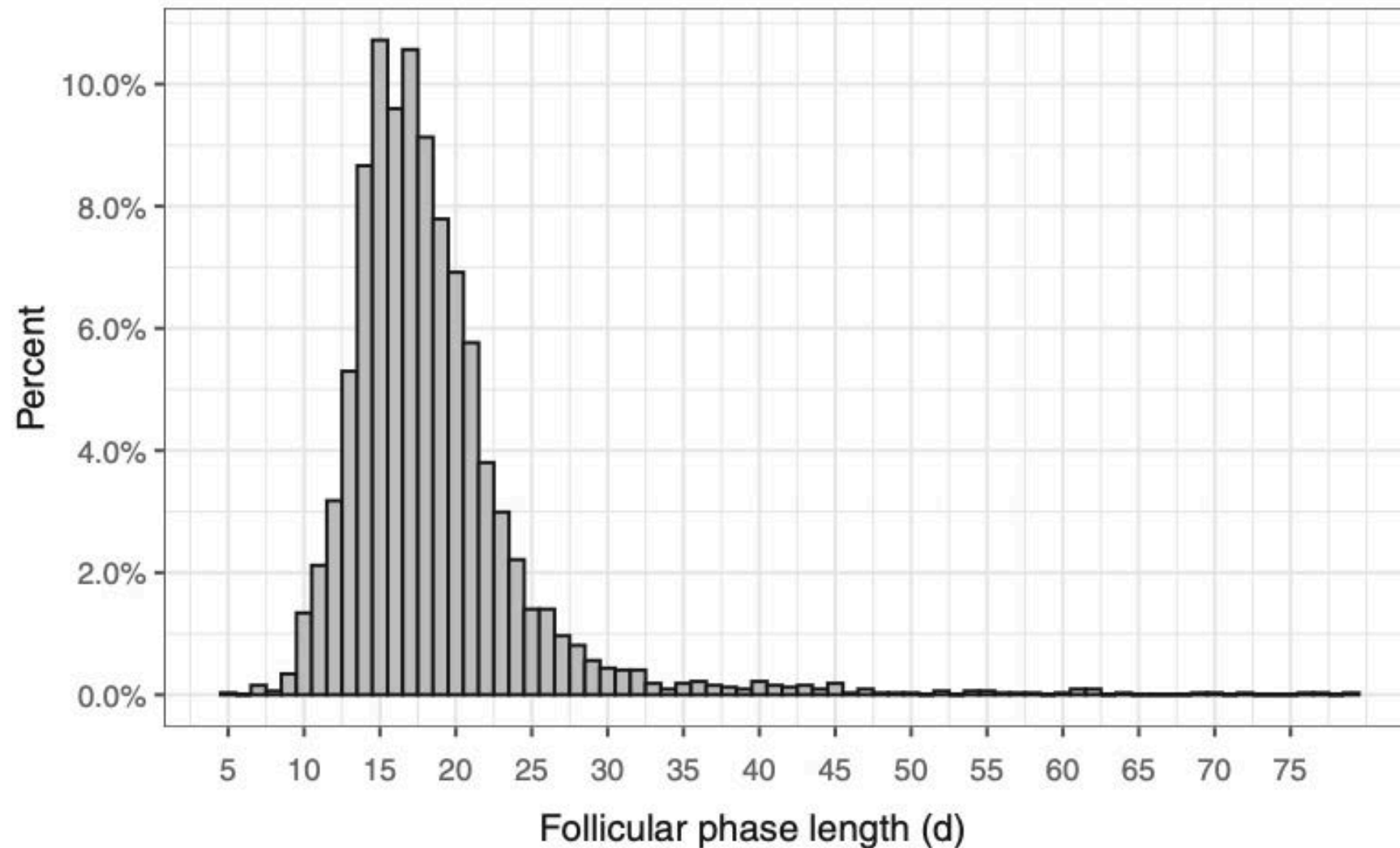
Najmabadi et al.
Paed Perinat Epidemiol 2020

On what day
of the cycle
does
ovulation
usually
occur?



The menstrual cycle: day of ovulation

(c) Distribution of follicular phase length
3209 ovulatory cycles, 577 women 18- to 40-y-old



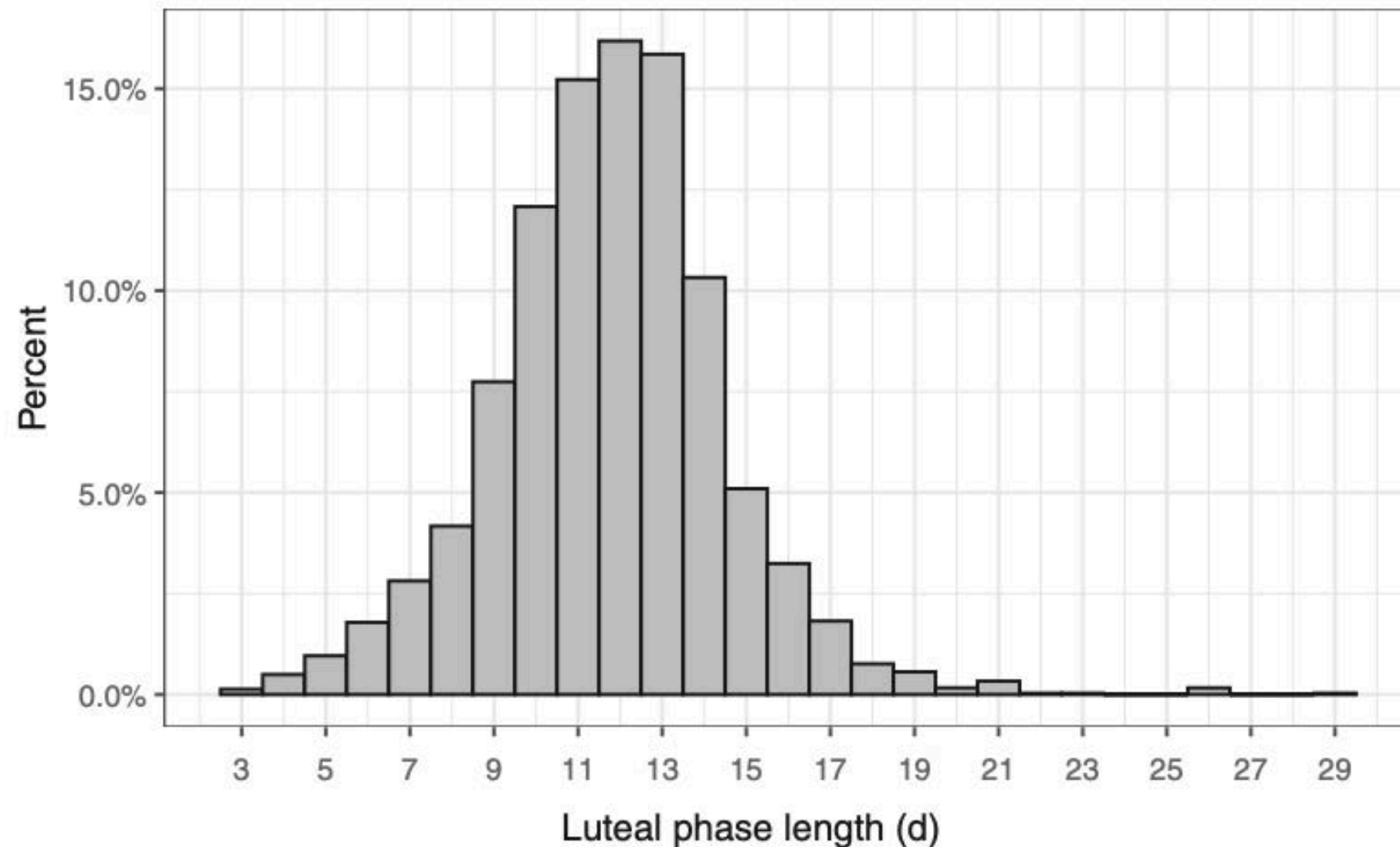
Najmabadi et al.
Paed Perinat Epidemiol 2020

What is the typical duration of the luteal (postovulatory) phase?

The menstrual cycle: luteal length

(d) Distribution of luteal phase length

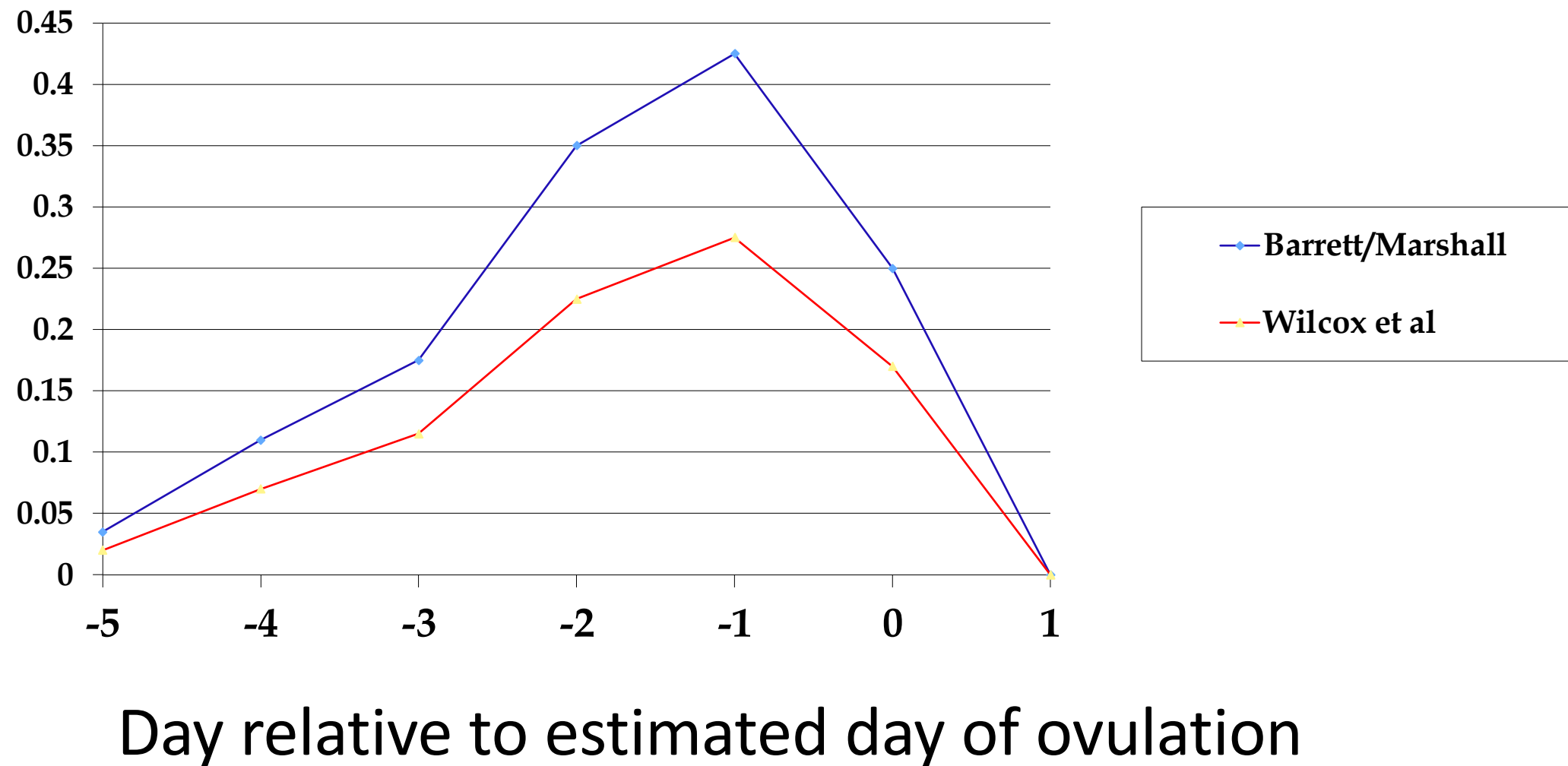
3022 non-conception ovulatory cycles, 555 women 18- to 40-y-old



Najmabadi et al.
Paed Perinat Epidemiol 2020

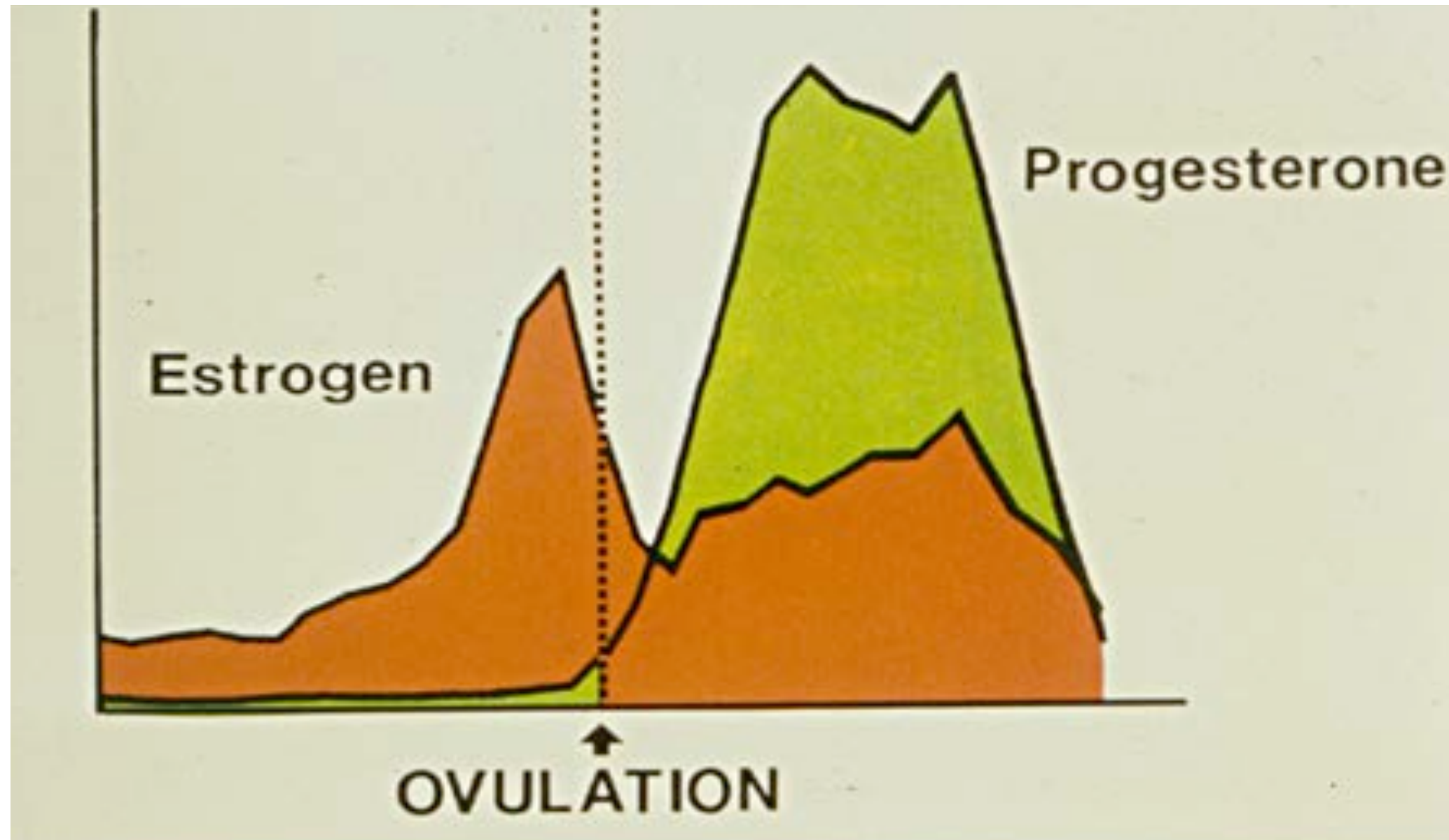
How many days during the menstrual cycle can a woman (couple) get pregnant?

Probability of clinical pregnancy

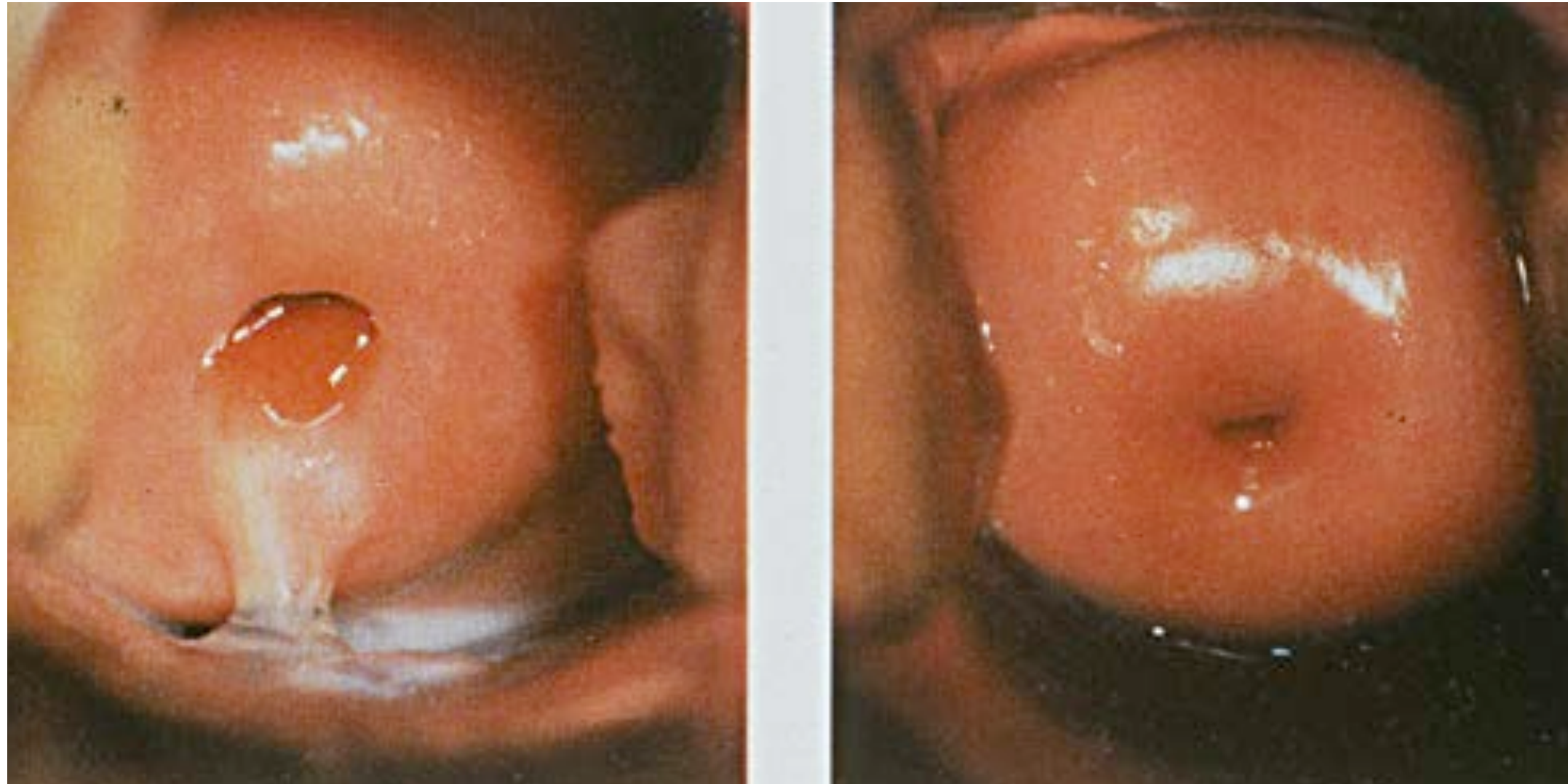


Dunson DB, et al. *Hum Reprod* 1999.

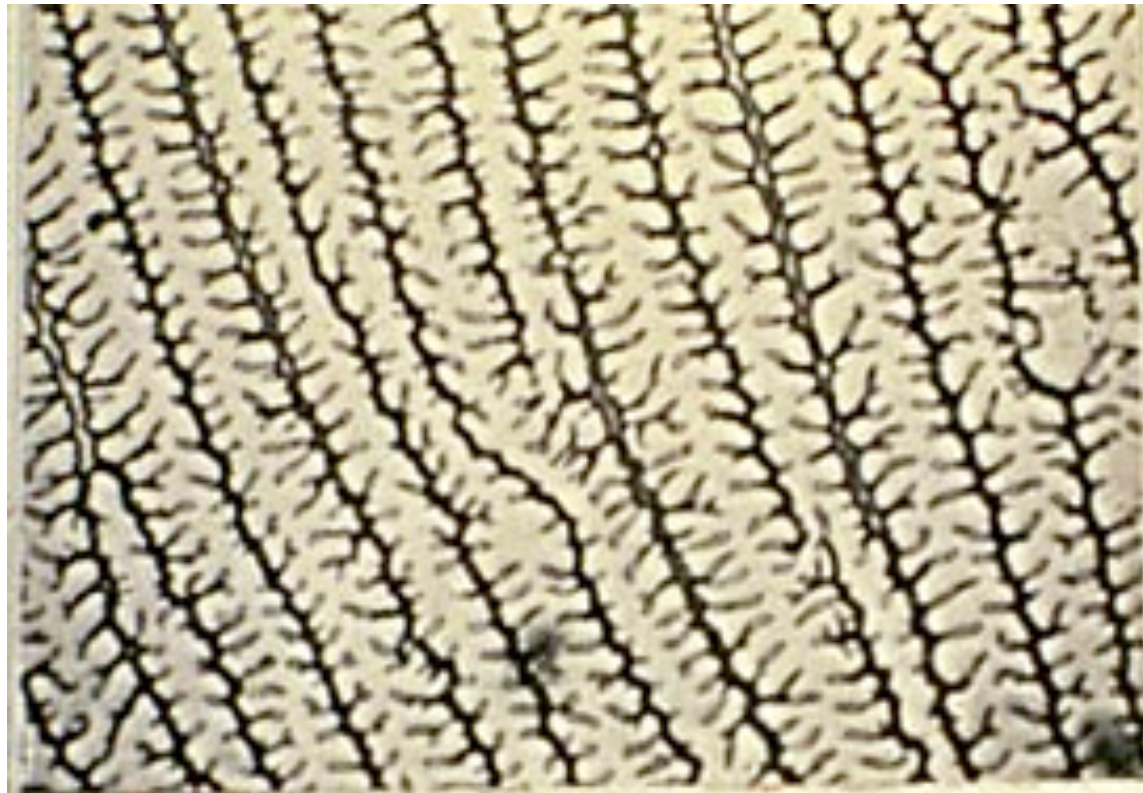
Ovarian hormones



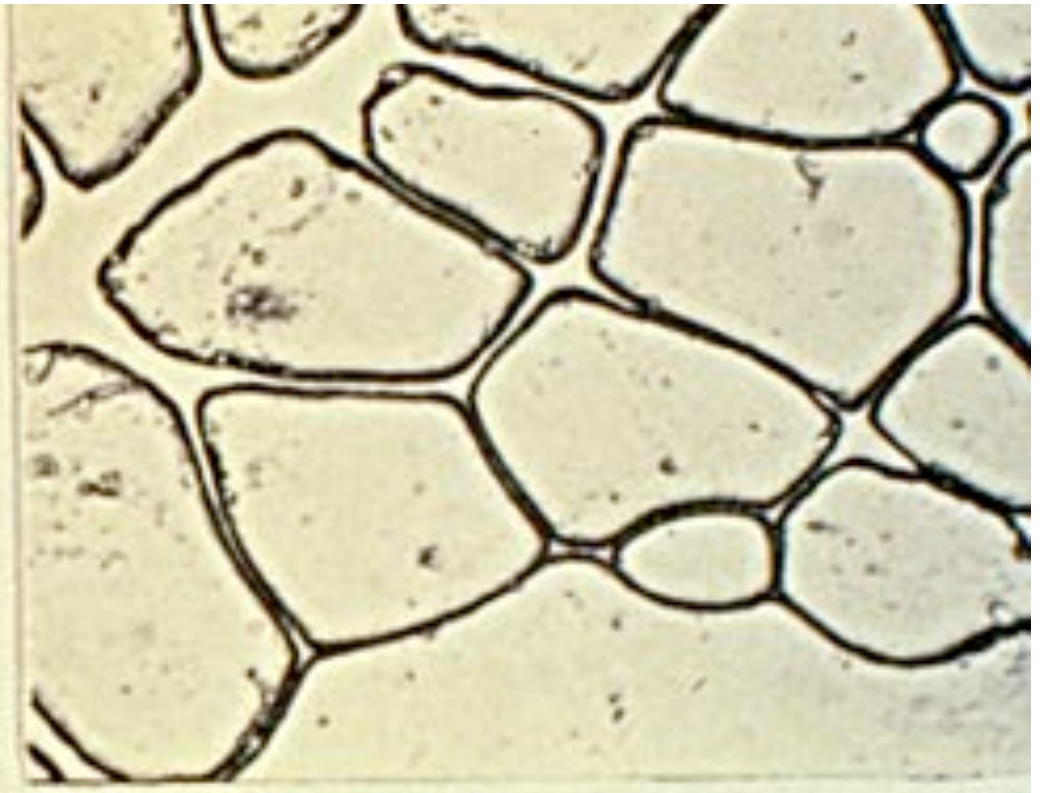
Type E and G mucus at the cervix



Type E and G mucus: light microscopy



TYPE E

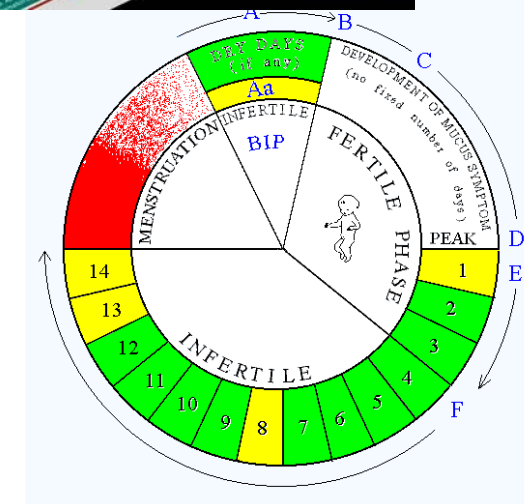
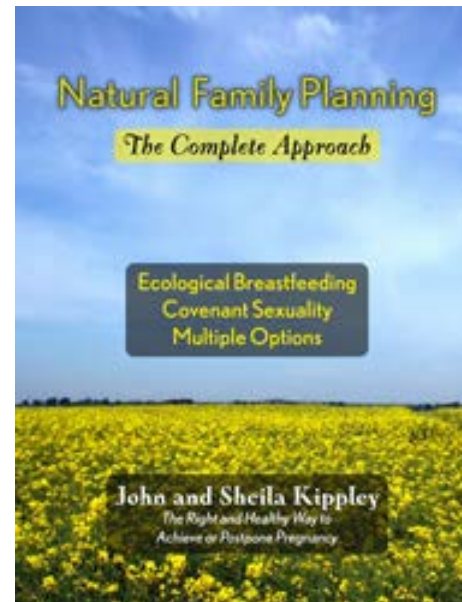
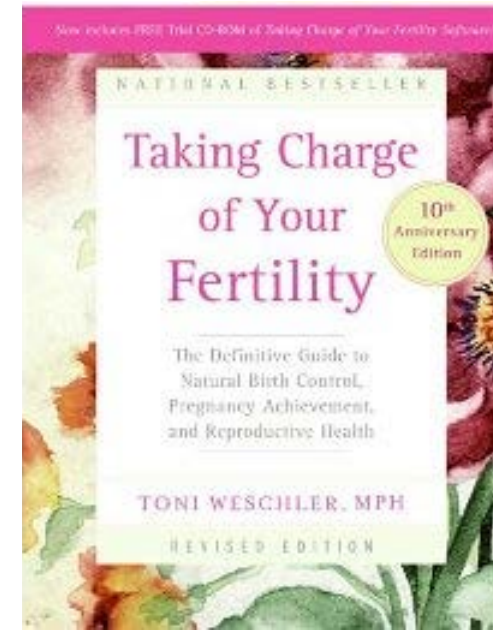


TYPE G

How can a woman identify her ovulation and fertile days?

Fertility awareness

Women and couples can learn to determine their fertile window by observing their own biomarkers.



Identifying the fertile window

- Before ovulation: mucus increases, rise in urinary estrogen, LH surge
- After ovulation: mucus decreases, basal body temperature rises, progesterone metabolites in urine

Fertility awareness- systems

- Standard Days (*cycle beads; only cycles 26-32 days*)
- Dynamic Optimal Timing (CLUE app)
- Urine LH tests (limited window)
- Peak Day Method (*google: Peak Day Utah*)
- Billings Method or Creighton method
- Marquette Method
- BBT (retrospective; NaturalCycles app)
- Sympto-thermal (*Kindara app; TCOYF; CCL*)

Fertility awareness in women trying to conceive

	No. of pregnancies	No. of cycles	Adjusted ^a	
			FR	95% CI
No fertility indicator	669	5,464	1.00	Ref
BBT only	7	44	1.39	0.71-2.70
Urine LH only	38	421	0.81	0.59-1.10
Cervical fluid only	10	147	0.61	0.32-1.16
Charting days only	675	3,984	1.35	1.23-1.49
Charting days and BBT	48	355	1.17	0.89-1.53
Charting days and urine LH	272	1,939	1.24	1.08-1.41
Charting days and cervical fluid	455	2,934	1.29	1.16-1.45
Charting days, BBT, cervical fluid	218	1,439	1.25	1.09-1.44
Charting days, cervical fluid, urine LH	363	2,153	1.48	1.31-1.67
Charting days, BBT, urine LH	77	605	1.12	0.89-1.41
Charting days, BBT, cervical fluid, u. LH	453	2,752	1.42	1.27-1.59
Other methods	48	375	1.07	0.80-1.43

Stanford et al.
Fertil Steril 2019

a= female age, race/ethnicity, gravidity, BMI, income, current smoker, education, partner education, prior hormonal birth control, hours of sleep per night, irregular cycles, history of infertility, prenatal supplement intake, marital status, intercourse frequency, history of benign gynecologic disorder, history of sexually transmitted infection, maternal problems getting pregnant

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Primary care approach to the infertile couple

- History
- Physical exam
- Initial laboratory

History

Woman

- Reproductive History
- Menstrual History
- GYN History, STIs
- Contraception History
- Major or Chronic Illness
- Family History
- Smoking, Alcohol
- Medications, Supplements
- Hirsutism, Acne
- Weight, Eating Patterns
- Coitus- Lubricants, Pain
- Toxic Exposures?

Man

- Reproductive History
- Mumps
- Major or Chronic Illness
- Urologic History
- Heat to Testicles
- Smoking, Drugs
- Medications, Supplements
- Erectile Function
- Family History
- Weight, Eating Patterns
- Toxic Exposures?

Physical examination

Woman

- Virilization
 - Acne, Hirsutism
- Body Mass Index
- Galactorrhea?
- Thyroid
- Pelvic Examination
 - Anatomic issue?
 - Pain?

Man

- Urologic Examination
 - Varicocele?
 - Hypospadias?

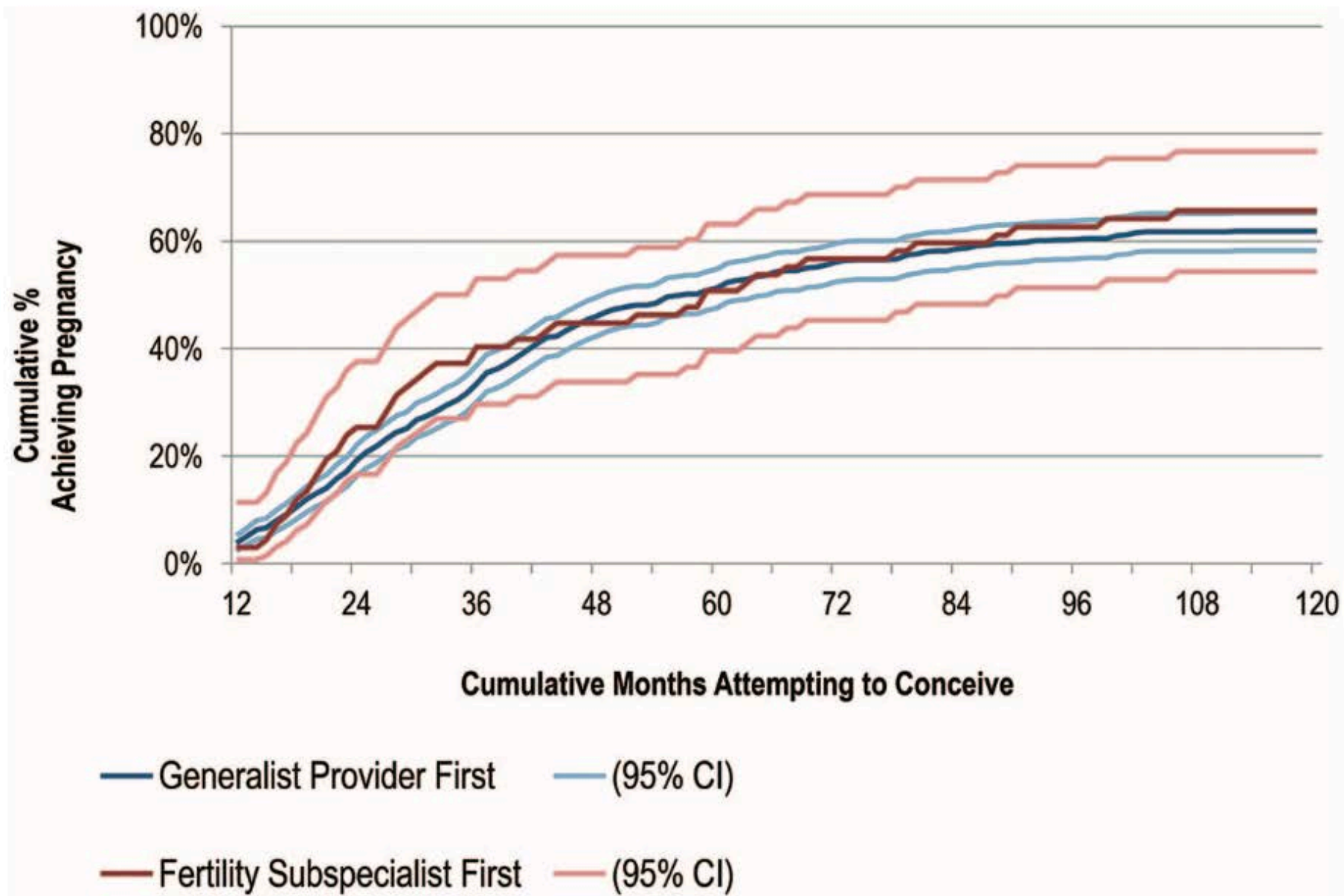
Initial laboratory

Woman

- **Assess ovulation, fertile window, cycle history**
- Hysterosalpingogram or chlamydia antibody
- Consider TSH, Prolactin
- Evaluate for metabolic abnormalities, **PCOS**

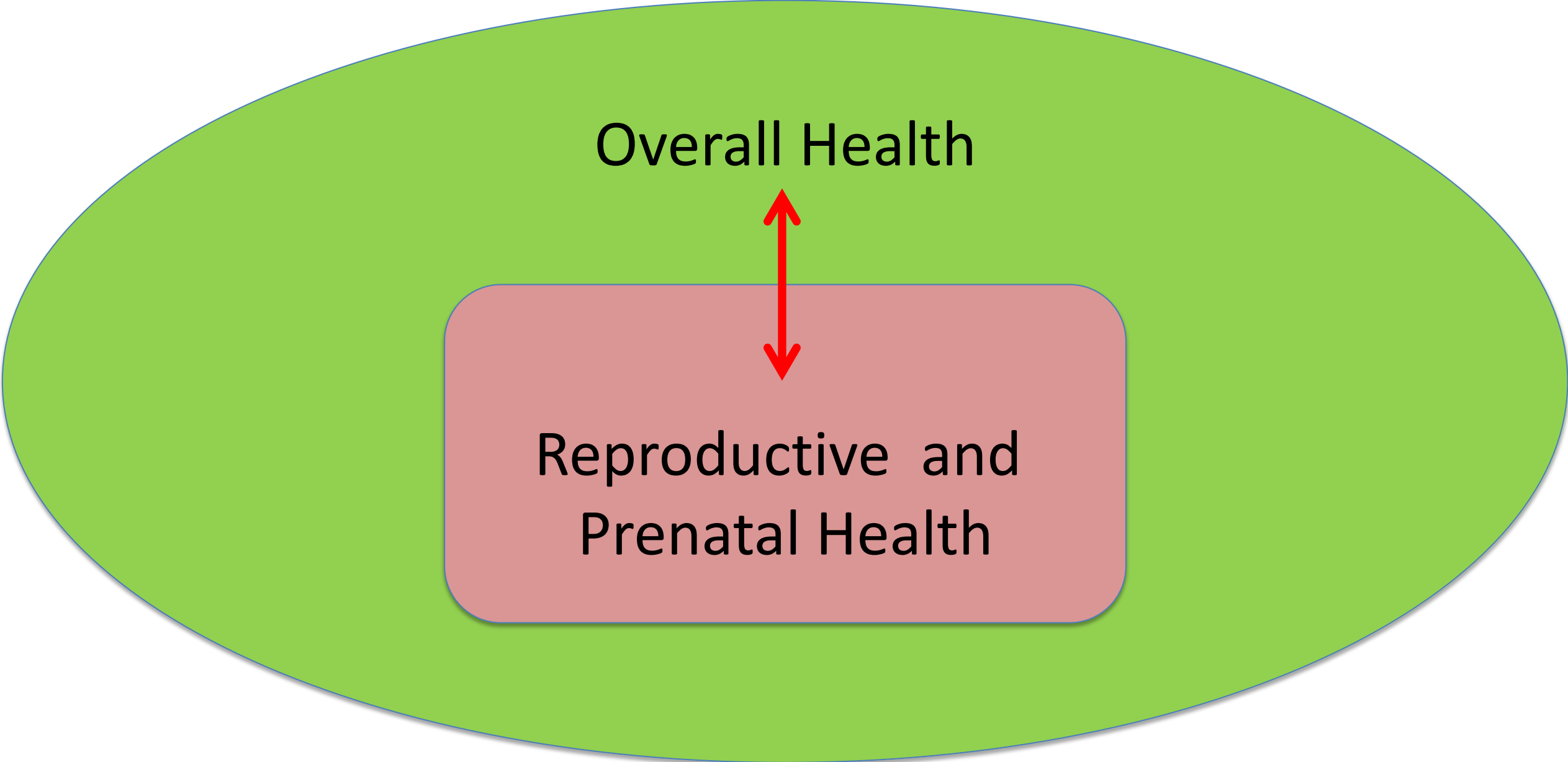
Man

- **Semen Analysis**
- Evaluate for metabolic abnormalities



Likelihood of receiving IVF: aOR 0.48 (0.10-0.59)

Restoring underlying health will often improve healthy reproduction



Overall Health

Reproductive and
Prenatal Health

Treatment

- Man: lifestyle counseling
 - If varicocele= urology referral
 - Treat underlying conditions
- Woman
 - Learn the cycle and the fertile window
 - Treat underlying conditions
 - PCOS
 - Overweight
 - Thyroid
 - Endometriosis (surgical referral)

Optimized cycles

- Ovulation
- At least one act of intercourse on the highly fertile days
 - 1-2 days prior to ovulation
 - Days of best quality mucus
- Luteal (postovulatory) phase at least 11 days
 - Can support with human progesterone (prometrium, NOT provera)
 - Check progesterone and estradiol levels *7 days after ovulation*
- No abnormal spotting/bleeding
- Psychosocial stress addressed!
- If no pregnancy in 6 optimized cycles, refer

Restored mom & dad --> healthier babies



Low birth wt

RRM

<5%

IVF

~9%

Prematurity

<5%

~15%

Stanford JB, Parnell TA, Boyle PC. J Am Board Fam Med 2008, 21:375-384.

Boyle PC, de Groot T, Andralojc KM, Parnell TA. Front Med (Lausanne) 2018;5:210.

Sart.org 2018 statistics

- Understanding the fertile window is fundamental to women's health.
- The fertile window is ~9 days (as identified) and can occur early, middle, or late cycle.
- Primary care should perform the first steps of fertility evaluation, and continue to follow the couple, especially for underlying health conditions.

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801-213-2996
- medicine.utah.edu/dfpm/public-health/research-service/ocrh/