



Polycystic Ovary Syndrome: medical management of infertility

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Conflict of Interest

External Industry Relationships *	Company Name	Role
Equity, stock, or options in biomedical industry companies or publishers	None	
Board of Directors or officer	None	
Royalties from Emory or from external entity	None	
Industry funds to Emory for my research	None	
Other	None	

What is infertility?

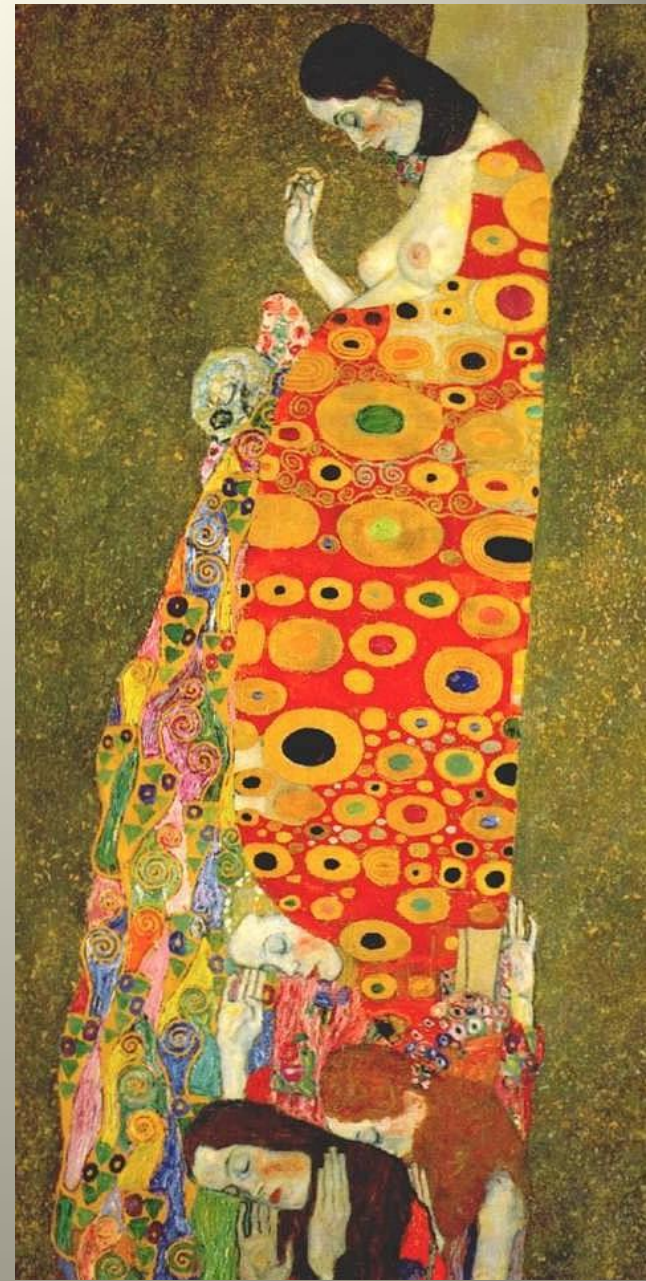


Edward Hopper, *Morning Sun*, 1952

- Normal conception rate per month in young women
 - 1st 20%, 3rd 50%, 6th 75%, 12th 90%
- Infertility is typically defined as one year of unprotected intercourse without conception (6 months if over 35)
- Occurs in 1 in 12 couples or 24 million women
- Women with PCOS often do not ovulate regularly

Complications in pregnancy that *may* be higher in women with PCOS

- Risk of miscarriage
- High blood pressure and preeclampsia
- Gestational diabetes
- Preterm delivery
- Cesarean delivery



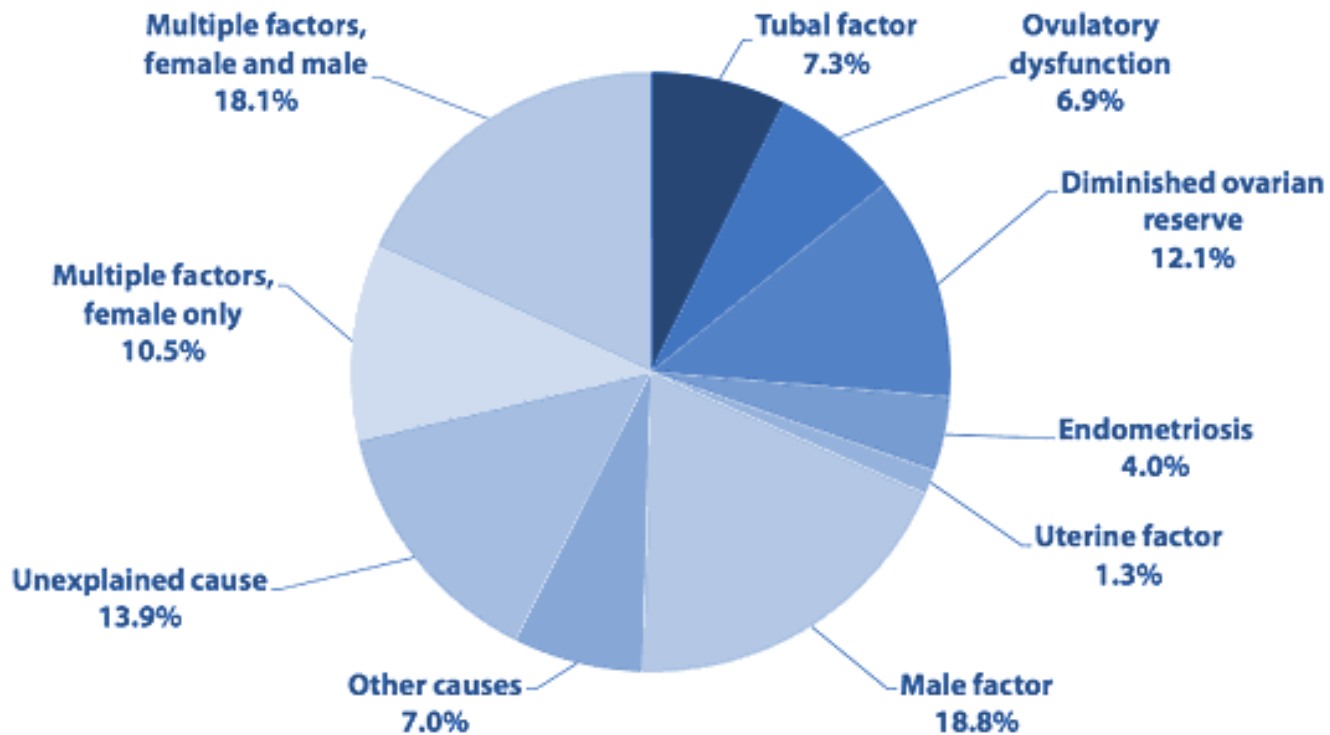
Gustav Klimt *Hope, II* 1907-8. MoMA

Recommended Testing

- Record menstrual pattern and check for ovulation
- Screen for metabolic problems that contribute to infertility and complications in pregnancy
 - diabetes/pre-diabetes, obesity, high blood pressure, thyroid disease
- Check the sperm
- Check the uterus and Fallopian tubes

Don't assume there are no other issues

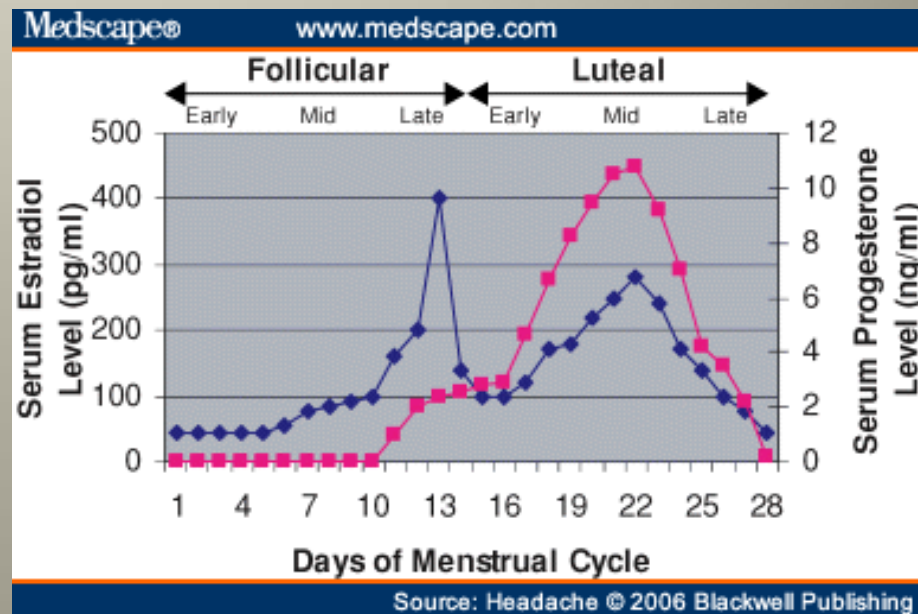
Infertility Diagnoses Among Patients Who Had ART Cycles Using Fresh Nondonor Eggs or Embryos*, 2010



* Total does not equal 100% due to rounding.

Detecting Ovulation

- Basal body temperature charting
- Urine ovulation predictor kits
- Progesterone level > 3ng/ml



Semen Analysis

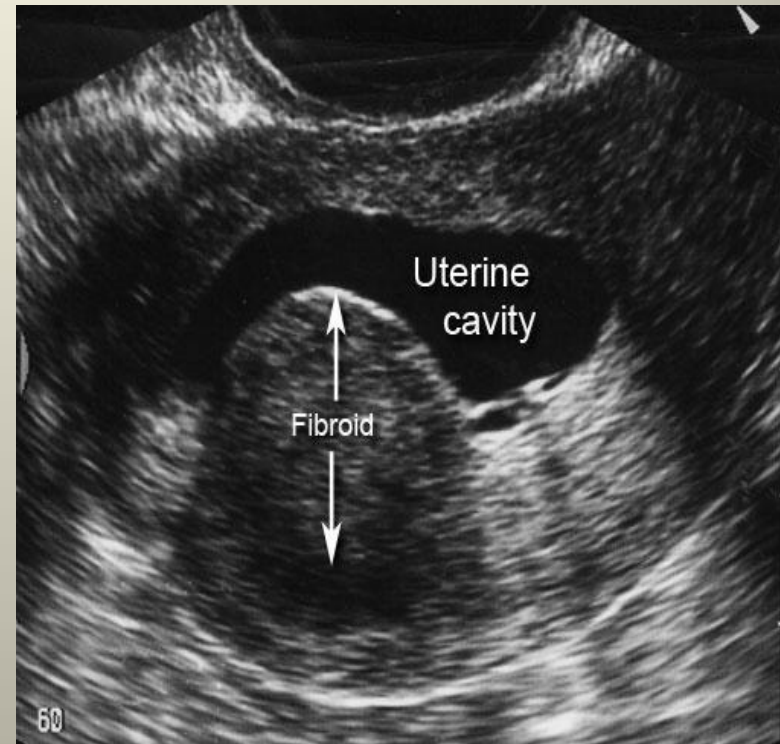
A microscopic view of several sperm cells, showing their heads, tails, and midpieces, scattered across the slide.

- Performed after 2-7 days of abstinence
- Avoid use of lubricants
- Collect at a fertility center or at home (bring in within one hour of collection)
- Abnormal tests should be repeated

Checking the Fallopian tubes and uterus



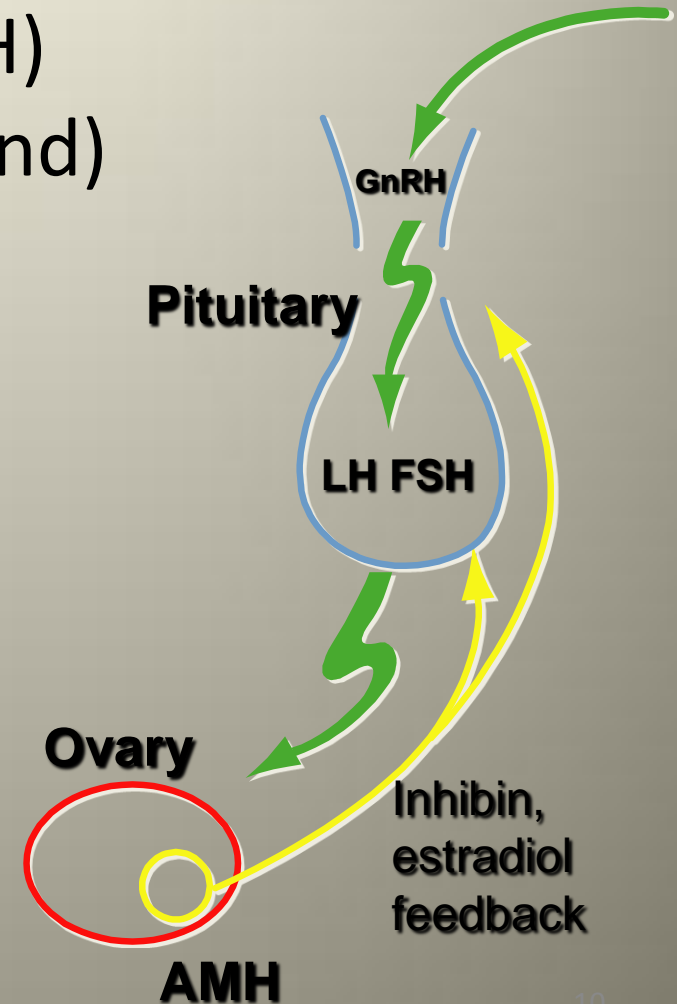
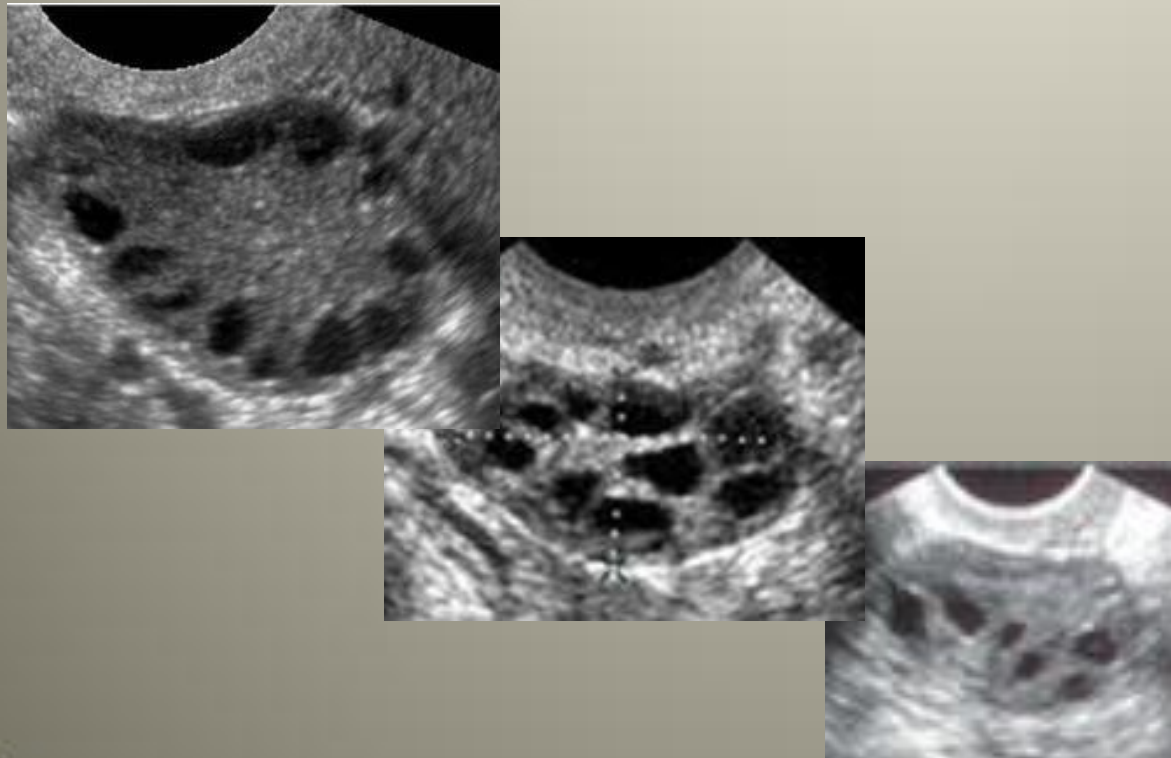
Hysterosalpingogram (HSG)



Sonohysterogram (SHG)

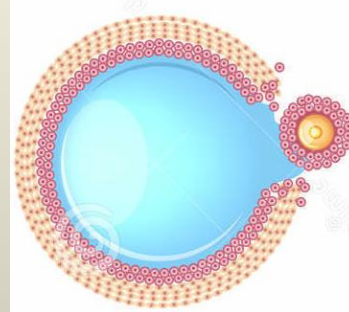
Ovarian Reserve Testing

- Day 3 FSH, estradiol (E_2)
- Antimullerian hormone (AMH)
- Antral follicle count (ultrasound)

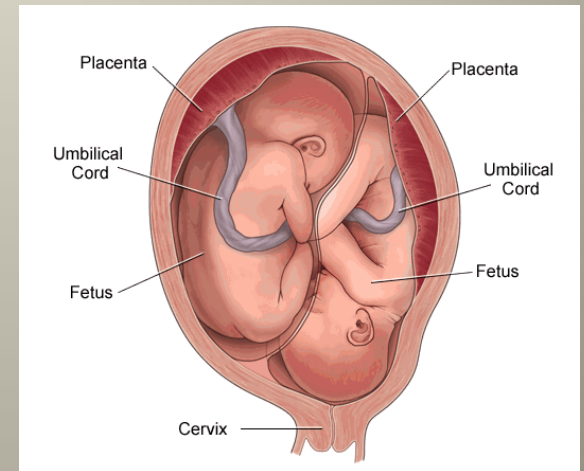


Goals of fertility treatment

- Restore ovulation
 - lifestyle changes
 - medications



- Minimize risk of multiple gestation



- Consider cost effectiveness



metformin (Glucophage)

- Who needs this?
 - Some doctors feel all women with PCOS benefit
 - Others treat only if pre-diabetic
- Benefits
 - May be more likely to ovulate
 - May lower miscarriage risk
 - May improve egg/embryo quality
- Risks
 - Gastrointestinal side effects common

Ovulation medications

2/3 of women respond to oral medications

- clomiphene citrate (Clomid), FDA approved
- letrozole (Femara), off label
- Risk of twins approximately 5-8%

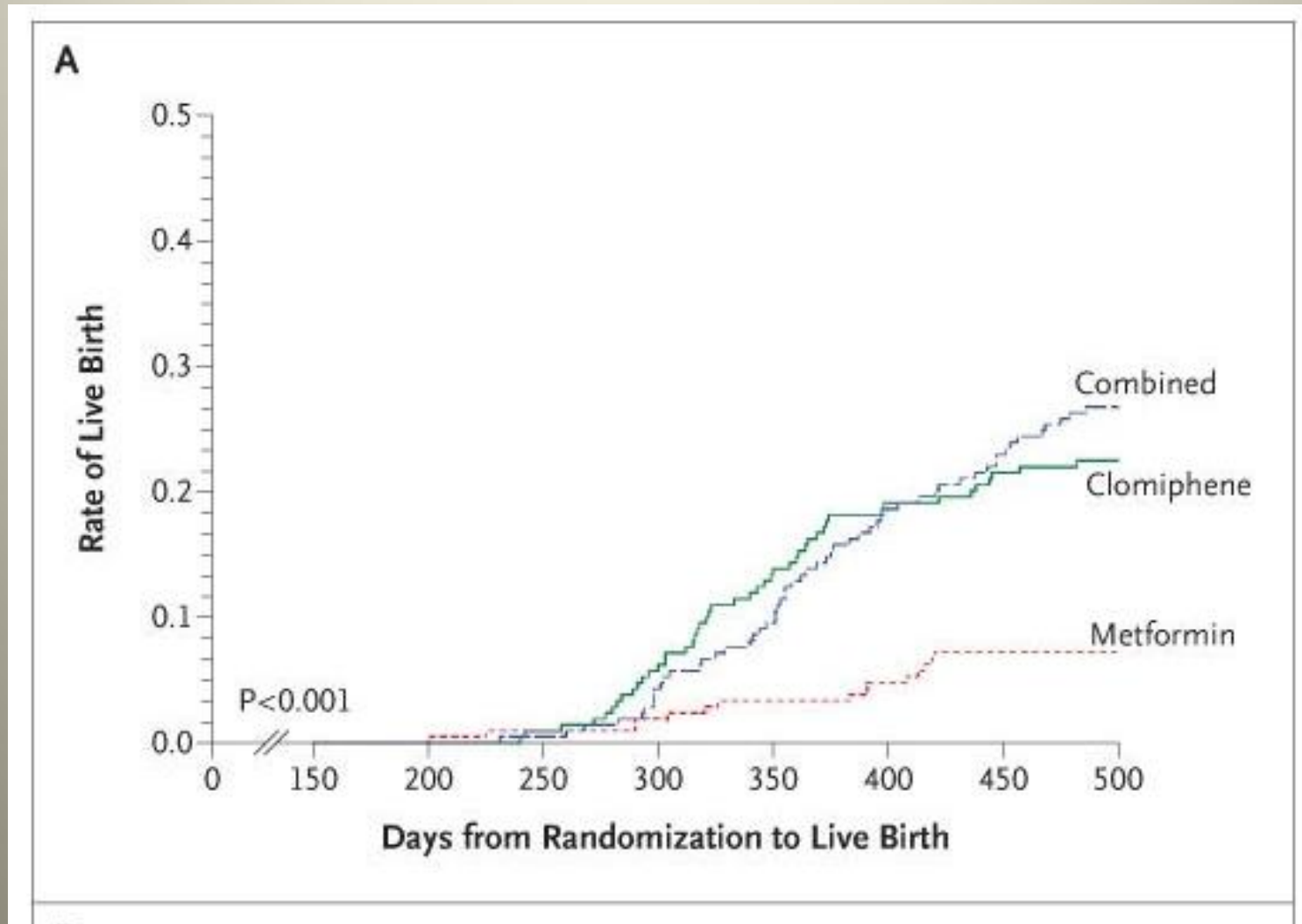


Gonadotropin injections: use lowest effective dose

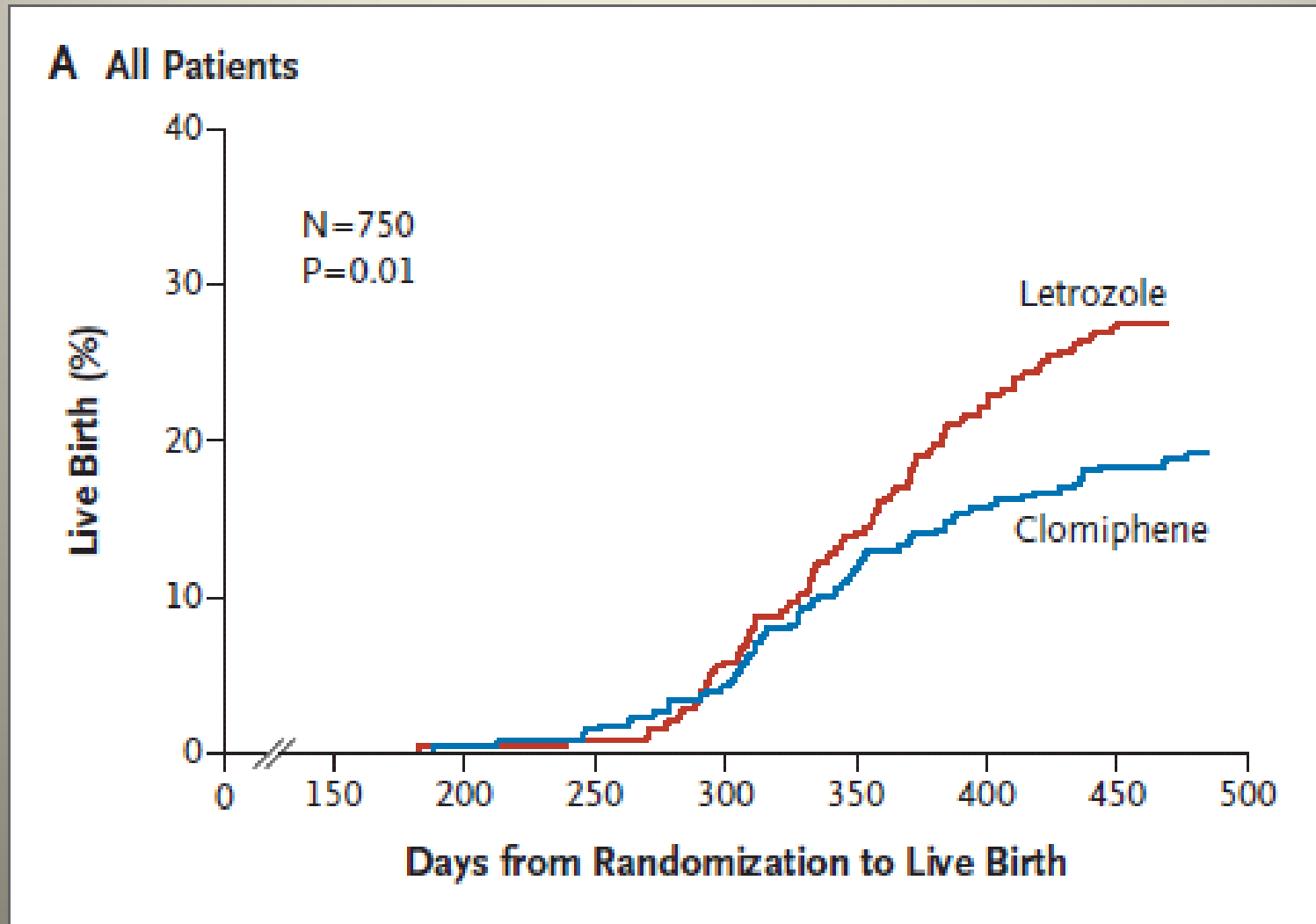
- More frequent monitoring with ultrasounds and blood tests
- Higher risk of multiple gestation



clomiphene, metformin or both?

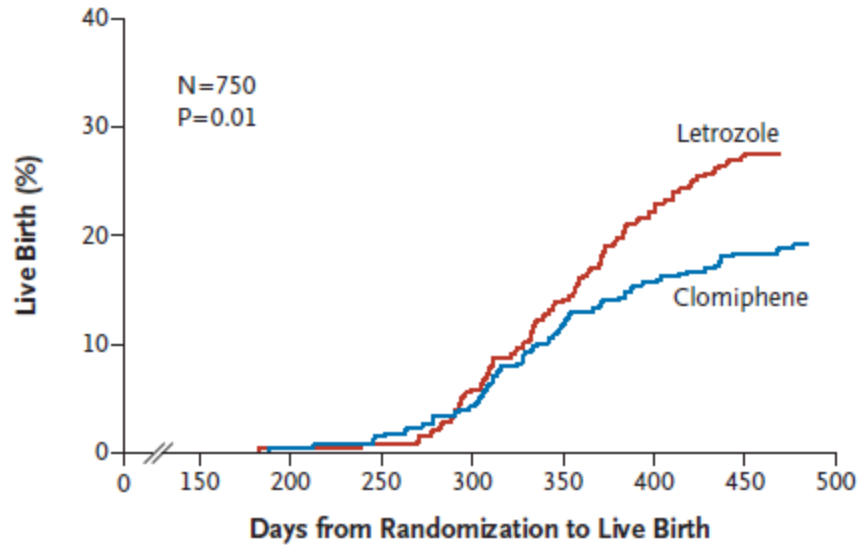


letrozole vs clomiphene in PCOS

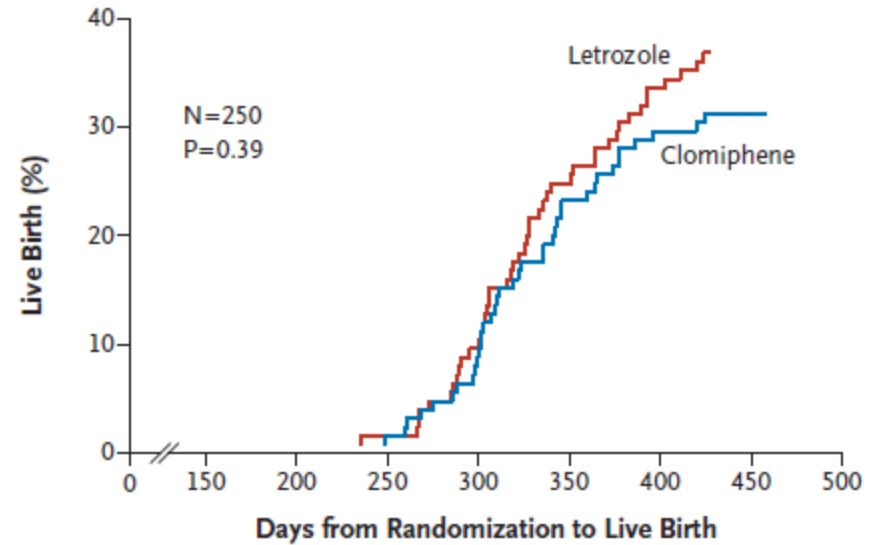


Letrozole may be more effective in obese women

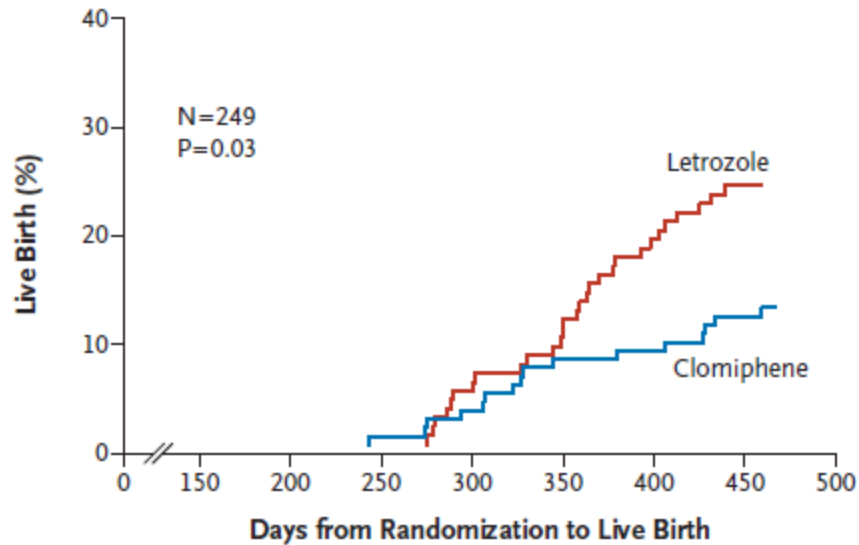
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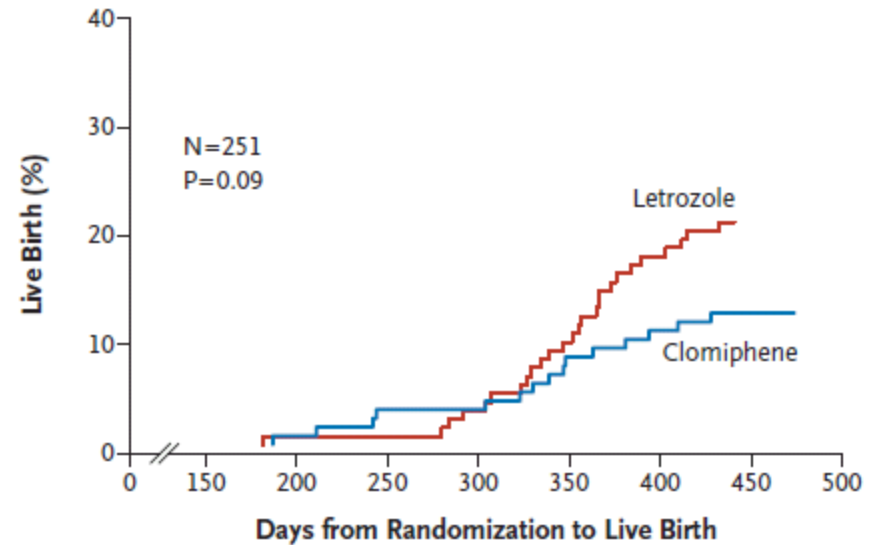
B BMI, ≤ 30.3



C BMI, >30.3 to ≤ 39.4

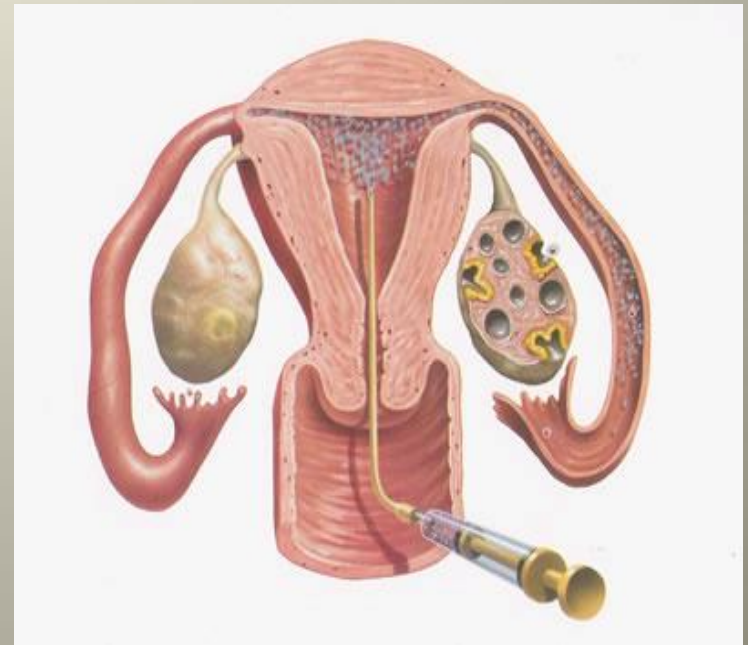


D BMI, >39.4



Intra-uterine insemination (IUI) may increase the chance of pregnancy

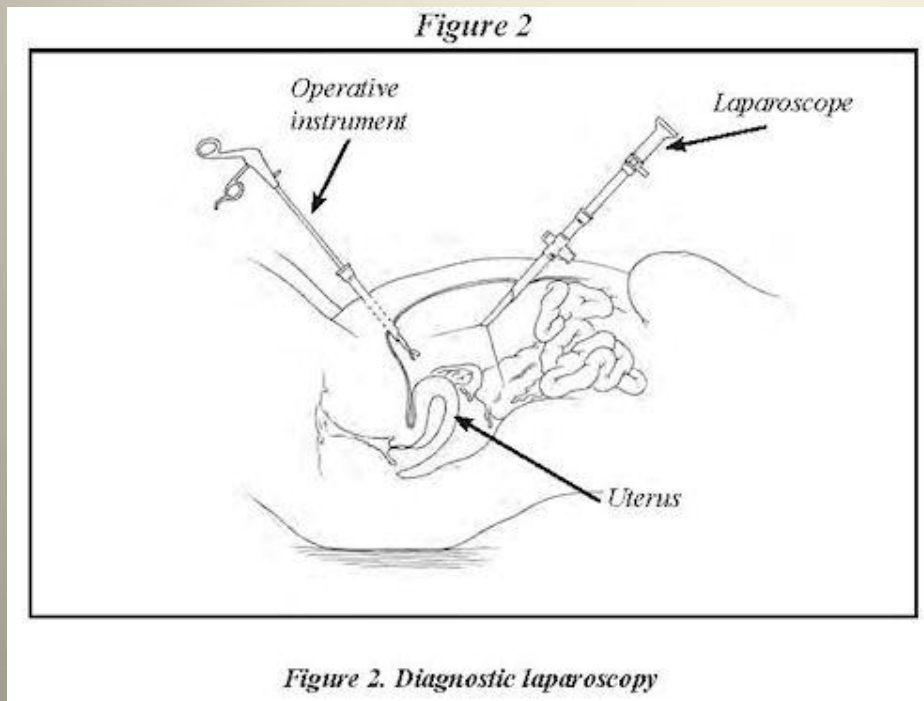
- Semen is washed and concentrated motile sperm are placed directly into the uterus near the time of ovulation
- For most women, feels like a pap smear
- Chance of pregnancy is approximately 10-18% per IUI



When to consider other options

- Not responding or over responding
- 3-6 cycles are reasonable in anovulatory women
- >6 cycles have very low chances of success
- >12 may be associated with a higher risk for ovarian cancer

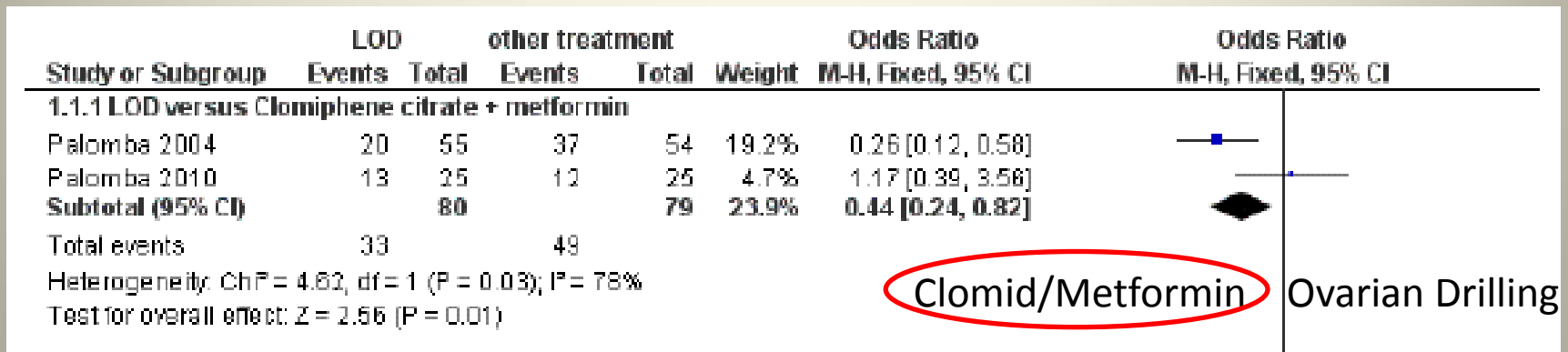
Laparoscopic ovarian drilling



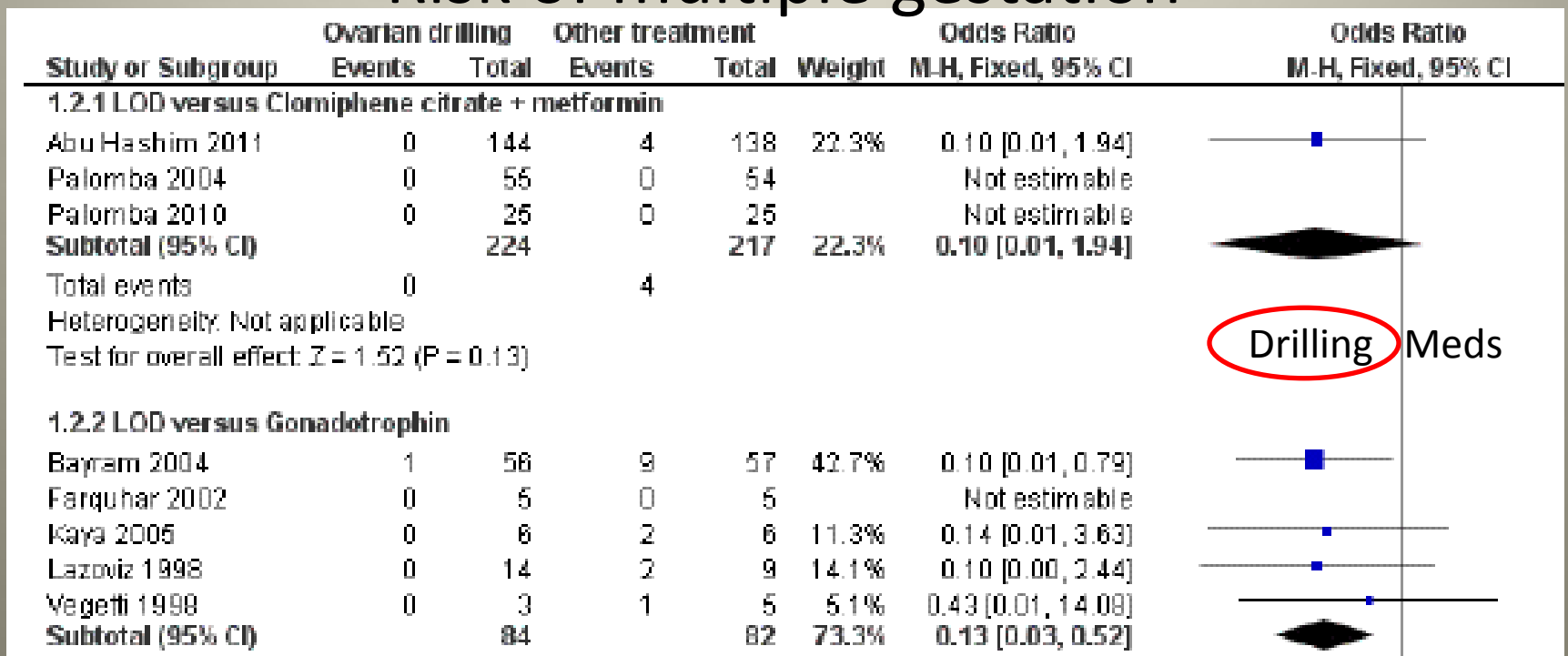
asrm.org

- Can help restore ovulation temporarily, typically not as effective as clomiphene and metformin
- Lowest risk for multiples
- Caution: may cause diminished ovarian reserve

Laparoscopic drilling vs Clomid/metformin



Risk of multiple gestation



When to consider IVF

- Young women who do not respond to oral medications
- Ovulation induction hasn't worked
- Age is a concern
- Other factors are at play (tubes, sperm)
- Preimplantation genetic screening is desired

In vitro fertilization (IVF)

- Daily injections (FSH) for two weeks to stimulate the ovaries to produce eggs (10-20)
- Frequent monitoring with ultrasound and estrogen levels
- Egg retrieval under sedation

Figure 1

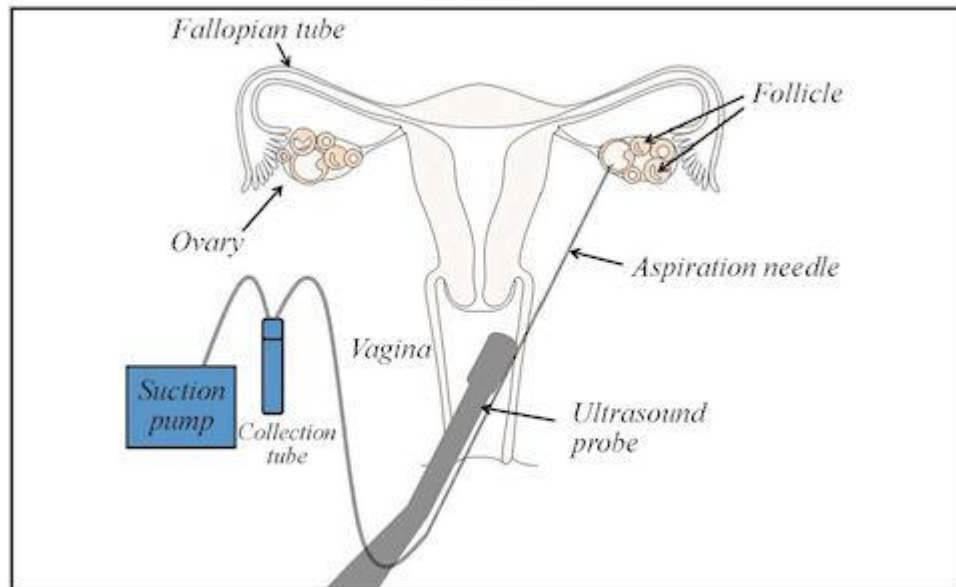
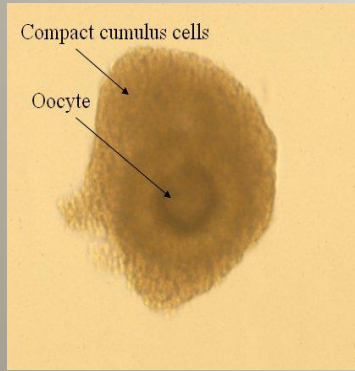


Figure 1. Egg retrieval is usually performed through the vagina with an ultrasound-guided needle.

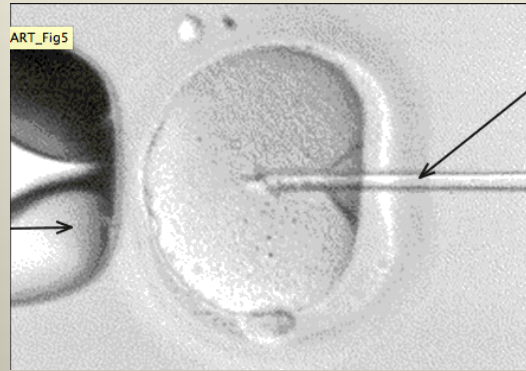


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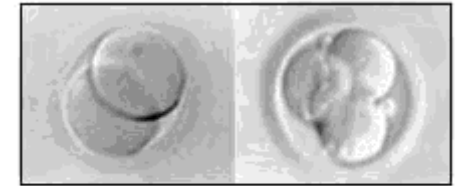
IVF lab procedures



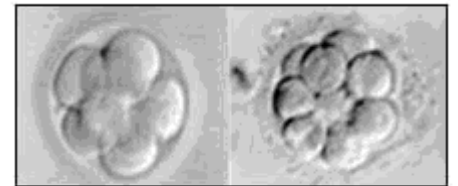
Eggs isolated



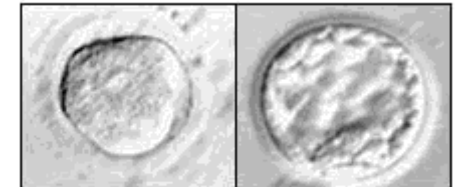
ICSI vs conventional insemination



Day 2



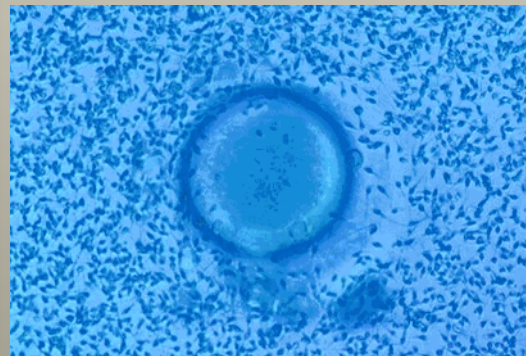
Day 3



Day 4

Day 5

Embryo culture



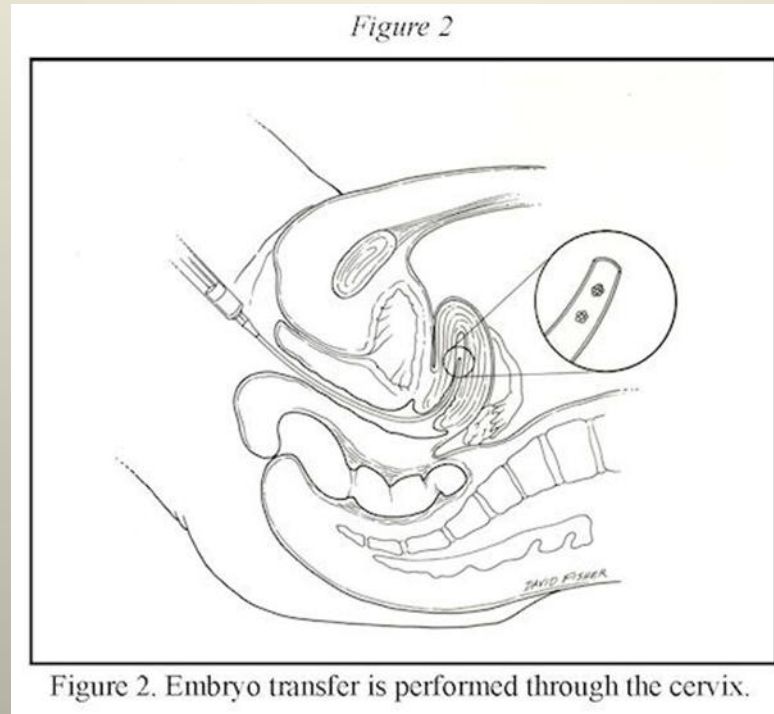
Preimplantation Genetic Diagnosis/Screening

Embryo



- Screen for genetic diseases before pregnancy
- Screen for chromosomal abnormalities that may lead to implantation failure and miscarriage

Embryo transfer



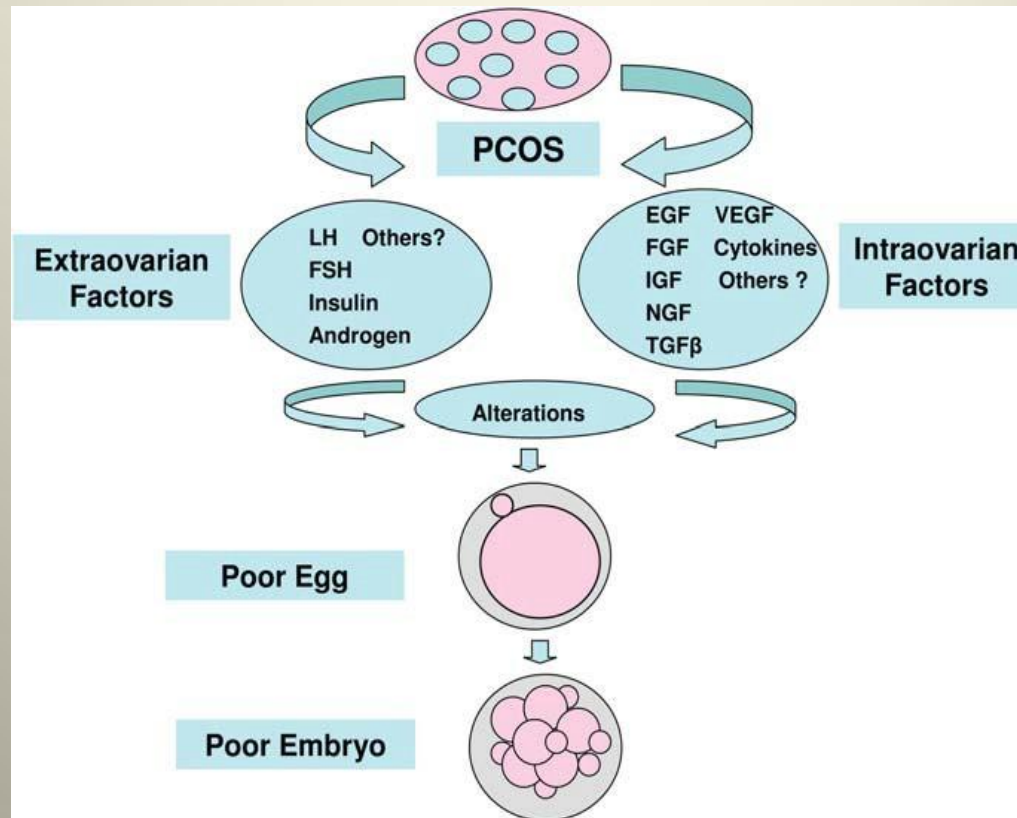
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- 3-5 days after egg retrieval
- Can also be done with frozen embryos
- No anesthesia, feels like a long pap smear

Risks of IVF with PCOS

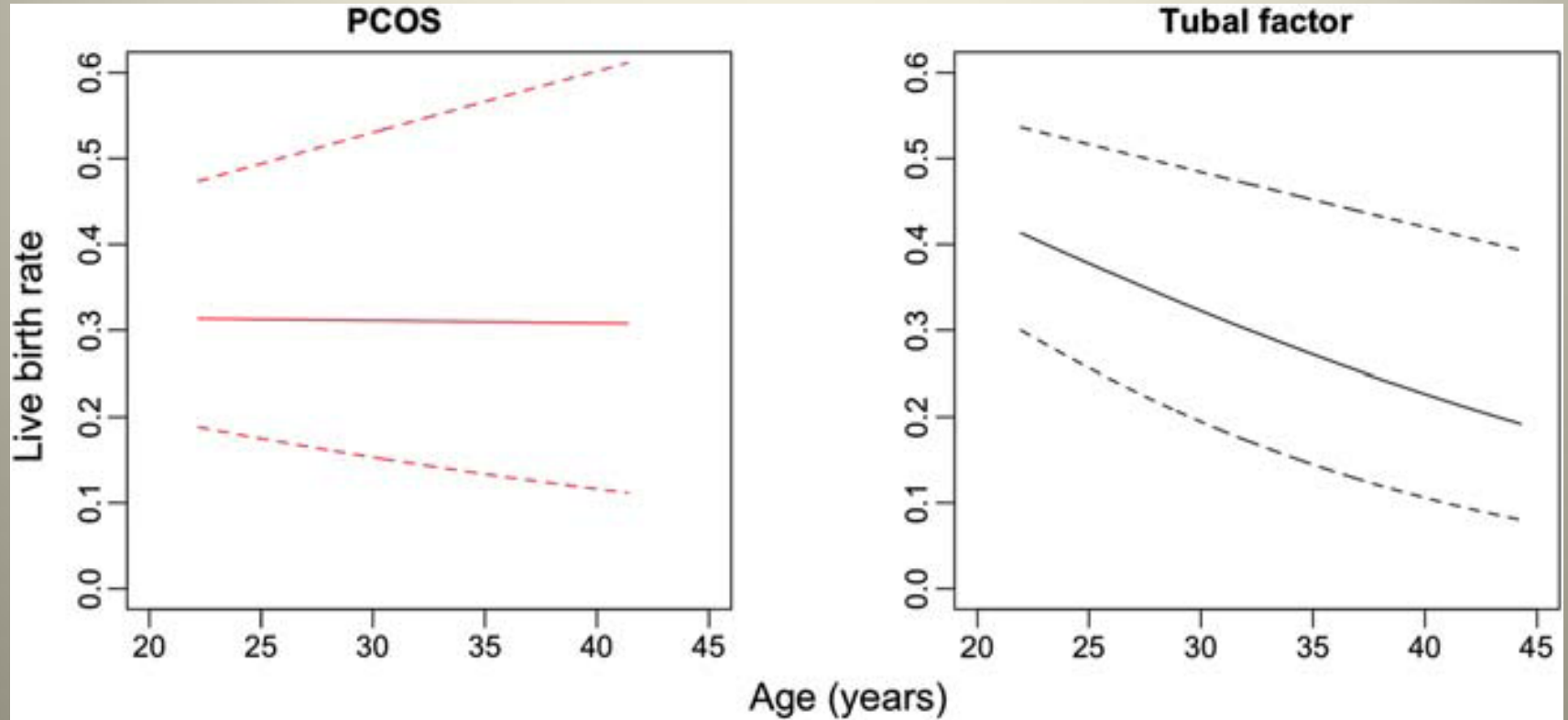
- Multiple gestation if more than one embryo is transferred
- Ovarian hyperstimulation syndrome (OHSS)
- Injury during egg retrieval if ovaries are difficult to access
- Its expensive!

Egg and embryo quality in PCOS



- *May* have poorer quality embryos and higher rate of miscarriages secondary to high LH, insulin and androgens
- Alterations in growth factors that help follicles grow may alter egg quality

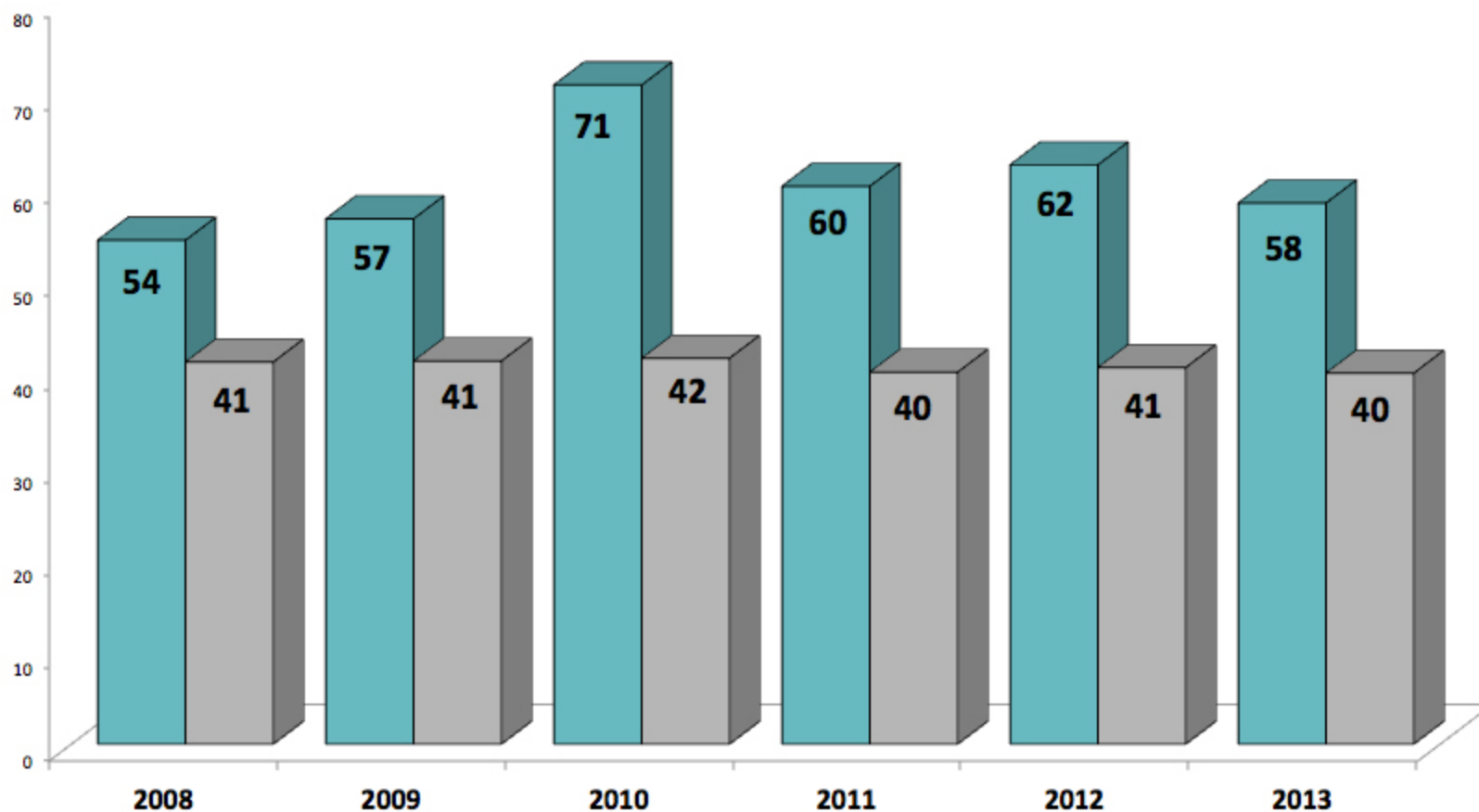
IVF and PCOS: the good news



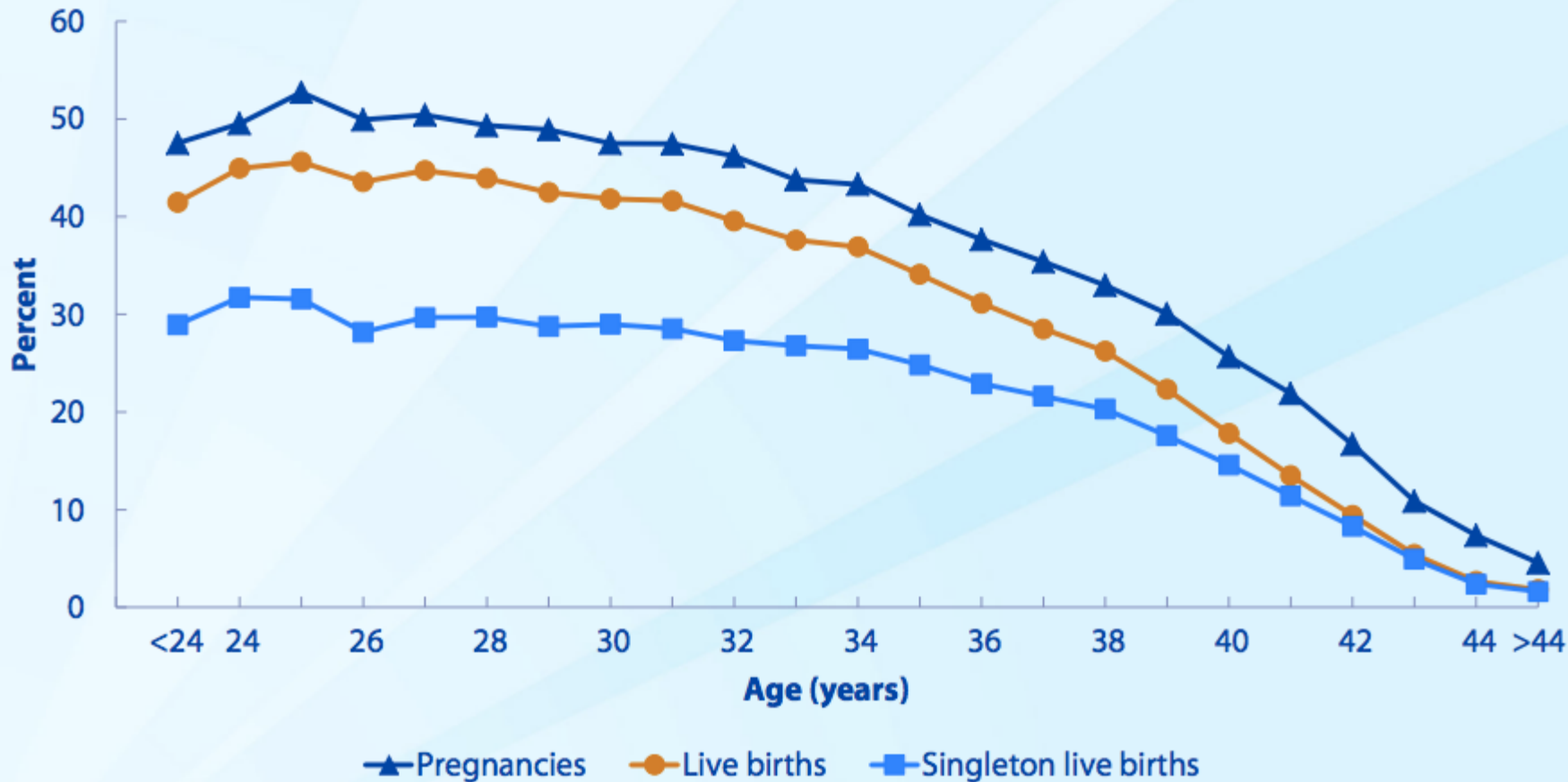
Predicted age-specific live birth rates for women with PCOS or tubal factor infertility **undergoing first treatment with IVF..**

Emory Reproductive Center vs. National Average IVF Success Rates, Women < 35 Years Old % of Cycles Resulting in Live Birth

■ Emory Reproductive Center ■ National Average



Percentages of ART Cycles Using Fresh Nondonor Eggs or Embryos That Resulted in Pregnancies, Live Births, and Singleton Live Births, by Age of Woman,* 2012



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Thank you!