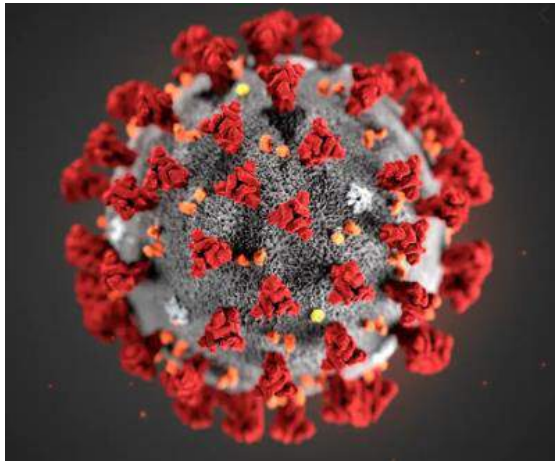
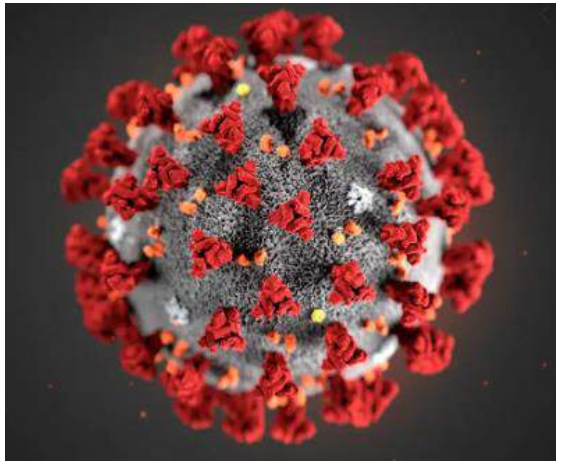
COVID-19 and IVF

"The New York City Experience"





Eric J. Forman, MD, HCLD
Medical & Laboratory Director
Columbia University Fertility Center
New York, NY

April 23, 2020

This webinar series is endorsed by IFFS.

Objectives

- To provide an overview of the impact on COVID-19 on IVF in the U.S.
  - ASRM guidance
  - Response from fertility providers
  - Patient response
- To discuss the changes in the infertility evaluation and treatment introduced by COVID-19
- To describe a path toward continuing safe fertility care during the pandemic
  - Role of testing
  - Measures to make clinics as “Covid-free” as possible

asrm
American Society for Reproductive Medicine

Impacting Reproductive Care Worldwide

Patient Management and Clinical Recommendations During the Coronavirus (COVID-19) Pandemic

As of March 17, 2020

ASRM Guidance

1. Suspend initiation of new treatment cycles, including ovulation induction, intrauterine inseminations (IUIs), in vitro fertilization (IVF) including retrievals and frozen embryo transfers, as well as non-urgent gamete cryopreservation.

2. Strongly consider cancellation of all embryo transfers whether fresh or frozen.

3. Continue to care for patients who are currently “in-cycle” or who require urgent stimulation and cryopreservation.

ASRM Guidance

4. Suspend elective surgeries and non-urgent diagnostic procedures.

5. Minimize in-person interactions and increase utilization of telehealth.

Note: This guidance will be revisited periodically as the pandemic evolves, but no later than March 30, 2020, with the aim of resuming usual patient care as soon and as safely as possible.

Recommendations affirmed on Match 30 and April 13

Task force formed to draft recommendation on strategies for prioritizing and resuming infertility treatment in the weeks ahead

Rationale for ASRM Guidance

- Aimed at guarding the health and safety of patients and providers
- Our social responsibility, as an organization and as a community of providers and experts, to comply with national public health recommendations and apply them to all reproductive settings during this unprecedented time
- To proactively do our share in blunting the impact of this pandemic, while recognizing the need to safeguard limited health infrastructure resources.

Newly formed group representing over 400 fertility specialists drafts letter to Ricardo Azziz and the ASRM COVID-19 Task Force

Fertility Providers' Response

- Criticize "little input sought from active providers in the development of these current guidelines"
- Vast majority of fertility centers are free-standing medical facilities that operate without hospital affiliation
- Describes measures taken to reduce disease transmission risk – no longer practicing "business as usual"
- Stresses that Infertility is a disease

Webinars, Webinars, and more Webinars

1. What is your opinion of the current ASRM covid guidelines?

Too strict	27%
Just about right	62%
Not strict enough	11%

2. If you have modified, what are your modifications?

Same as before/no change	4%
Screen patients for symptoms	29%
Mask for all patients entering	4%
Office closed for non emergent visits	54%
Office closed	9%

3. As of today, are you following the ASRM guidelines no new cycle starts?

Yes	87%
No	13%

- Group of 35 reproductive epidemiologists strongly support ASRM guidance
- “ We contend that no REI provider should continue care that is not in complete compliance with the ASRM Taskforce guidance to stop all new treatment and continue limited care only for completing in-cycle patients or providing urgent stimulation and cryopreservation for rare cases”
- “In short, ASRM’s quick and aggressive guidance should be applauded for its wisdom to mitigate loss of life across the country”

Response from patients

change.org Start a petition My petitions Browse Membership Log in

Fight for women's rights to fertility treatment and evaluation

Beverly Reed started this petition to American Society of Reproductive Medicine and 1 other

20,070 have signed. Let's get to 25,000!

Ryan Weathers signed 2 minutes ago

Melisa Stokke signed 12 minutes ago

First name

Last name

Email

Brooklyn, 11216
United States

Display my name and comment on this petition

Response from patients

- Petition with >20,000 signatures
- We were stunned that the ASRM guidelines called for an essential shut down of all fertility treatment and evaluation
- Fertility treatment is both necessary and time sensitive
- Different parts of the country are seeing COVID-19 at different rates and over different timelines
- To conclude, we believe that the ASRM COVID-19 recommendations violate the principles of justice, autonomy, and nonmaleficense.

Mixed Messages in the (Social) Media

Dr. Oz says couples should have sex while quarantining

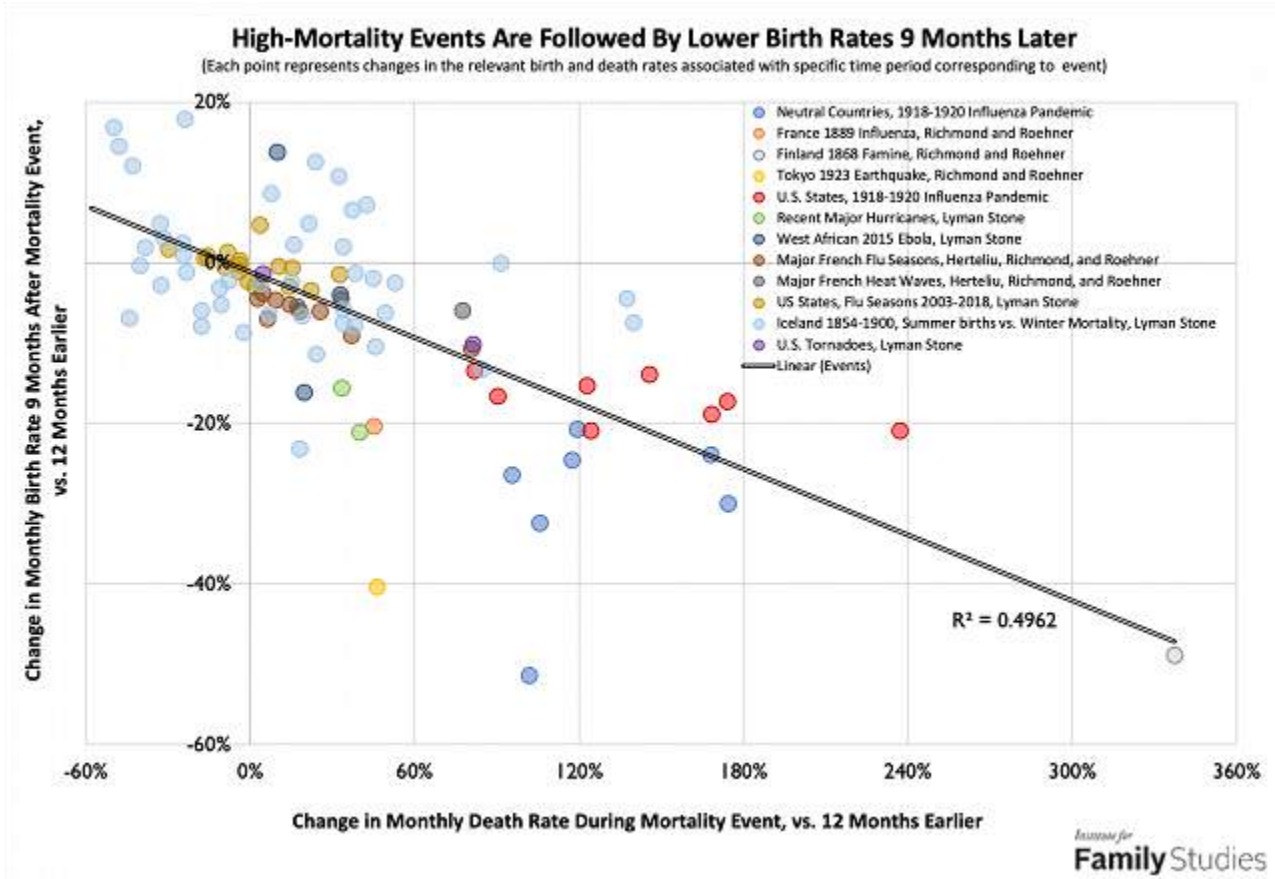
By Marisa Dellatto

March 17, 2020 | 7:11pm | Updated

Everyone's out here gearing up to stay inside from the **Coronavirus**, but forgetting the most crucial part...

2020-2021 **baby boom**, coming soon.

Baby Boom is Unlikely
Birth rates tend to decline but rebound later



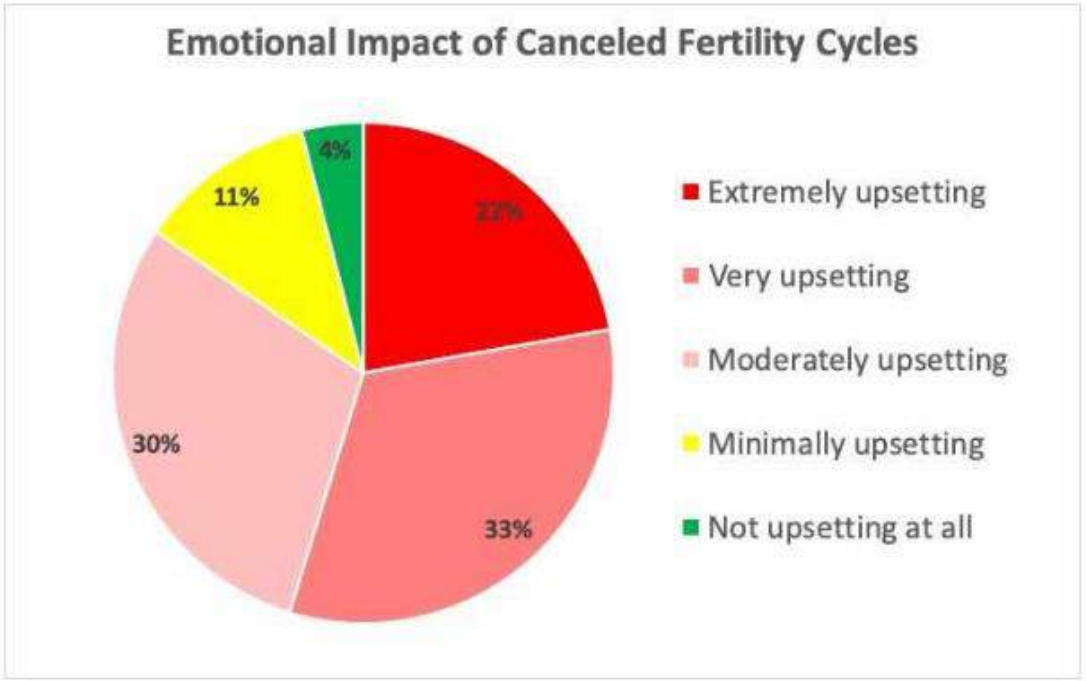
FERTILITY RATE AFTER CRISIS

DECREASE

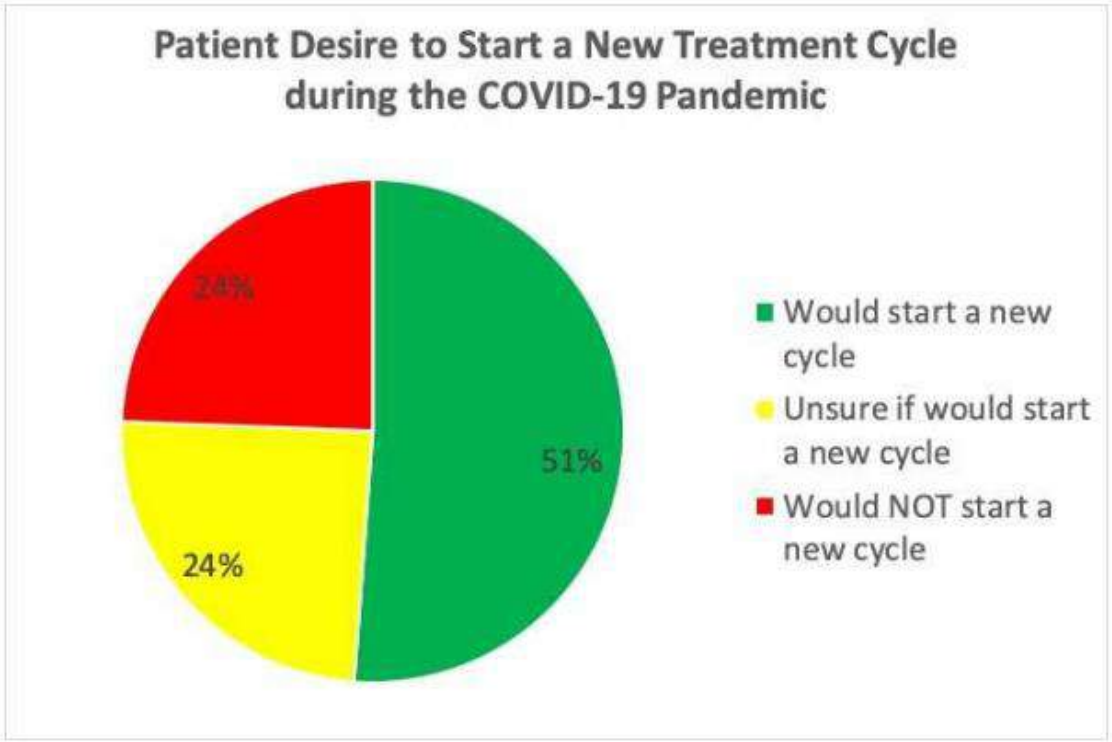
- Maternal mortality
- Neonatal mortality, pregnancy loss, preterm birth
- Behavioral
  - Fear of infection
  - Not wishing to infect spouse
  - Spousal sickness or death
  - Economic hardship
  - Stress on marriage
- Biological
  - Failure to conceive due to illness

INCREASE

- Behavioral
  - Household Isolation
  - "Recuperative fertility"
    Fear and trauma of loss motivating couples to conceive



Emotional impact of cancelled fertility cycles due to COVID-19 on patients. Extremely upsett was defined as the equivalent of the loss of a child.

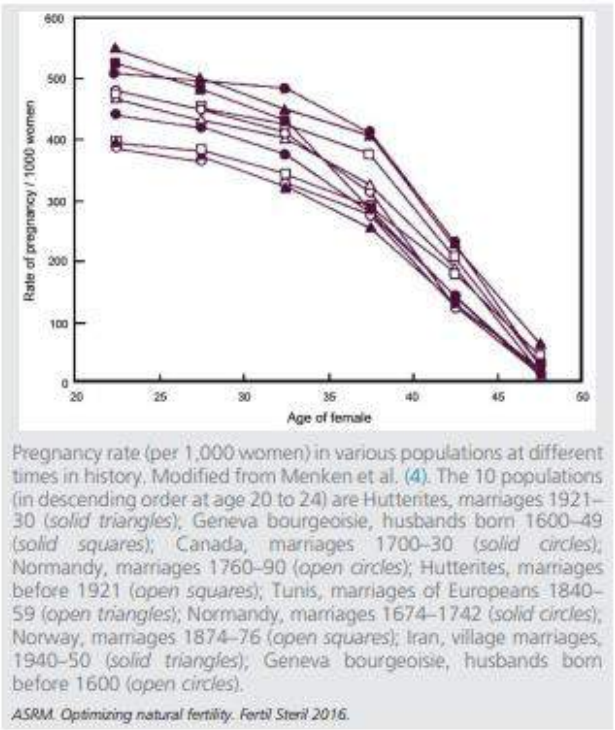


Fertility patients' desire to start a new cycle during the COVID-19 pandemic

Survey of 518 Columbia University Fertility Center patients, nearly half had a cycle canceled due to COVID-19

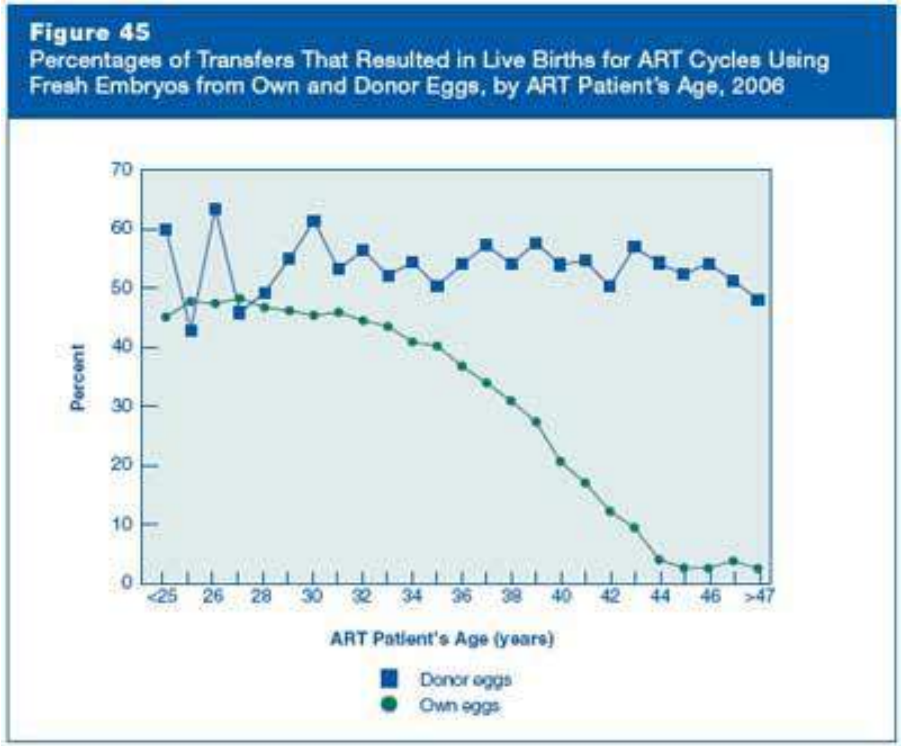
Does a fertility treatment pause affect outcomes?

Years matter – especially after age 37-38



Pregnancy rate (per 1,000 women) in various populations at different times in history. Modified from Menken et al. (4). The 10 populations (in descending order at age 20 to 24) are Hutterites, marriages 1921–30 (*solid triangles*); Geneva bourgeoisie, husbands born 1600–49 (*solid squares*); Canada, marriages 1700–30 (*solid circles*); Normandy, marriages 1760–90 (*open circles*); Hutterites, marriages before 1921 (*open squares*); Tunis, marriages of Europeans 1840–59 (*open triangles*); Normandy, marriages 1674–1742 (*solid circles*); Norway, marriages 1874–76 (*open squares*); Iran, village marriages, 1940–50 (*solid triangles*); Geneva bourgeoisie, husbands born before 1600 (*open circles*).

ASRM. Optimizing natural fertility. Fertil Steril 2016.



Does a fertility treatment pause affect outcomes?

- FORT-T Trial has been quoted to suggest months may not matter

Clinical pregnancy and live birth rates per couple, by randomization assignment for the first two treatment cycles and at the end of all treatment.

		First two treatment cycles		Duration of study	
Randomized treatment arm	No. of couples (%)	No. of clinical pregnancies[a,b] (%, 97.5% CI)	No. of live births[c] (%, 97.5% CI)	No. of clinical pregnancies[d] (%, 97.5% CI)	No. of live births[d] (%, 97.5% CI)
CC/IUI	51 (33.1)	11 (21.6, 10.2–37.3)	8 (15.7, 6.2–30.5)	38 (74.5, 58.4–86.9)	25 (49.0, 32.9–65.2)
Gonadotropin (FSH)/IUI	52 (33.8)	9 (17.3, 7.3–32.2)	7 (13.5, 4.9–27.6)	34 (65.4, 49.0–79.5)	22 (42.3, 27.1–58.7)
Immediate IVF	51 (33.1)	25 (49.0, 32.9–65.2)	16 (31.4, 17.7–47.9)	38 (74.5, 58.4–86.9)	24 (47.1, 31.2–63.4)
Total[e]	154	45 (29.2, 21.3–38.2)	31 (20.1, 13.4–28.4)	110 (71.4, 62.5–79.3)	71 (46.1, 37.0–55.4)

Note: Includes treatment-independent pregnancies. CC = clomiphene citrate; CI = confidence interval; FSH = follicle-stimulating hormone; IUI = intrauterine insemination; IVF = in vitro fertilization.

- RCT may not reflect real world conditions
  - Lower risk of drop out
  - Coverage for up to 6 egg retrievals
  - Some insurances require 3-6 IUI cycles prior to approving IVF
  - Clinics that stayed open report 40% decrease in volume

Goldman MB et al, Fertil Steril 2014

Follow

Alan Penzias
@AlanPenzias

Fertility Doc. Believer in ethical evidence based medicine. The gray whiskers and opinions are my own

Boston, MA bostonivf.com Joined April 2014

When and why does the dream die? Or does it?

Alan S. Penzias, M.D.

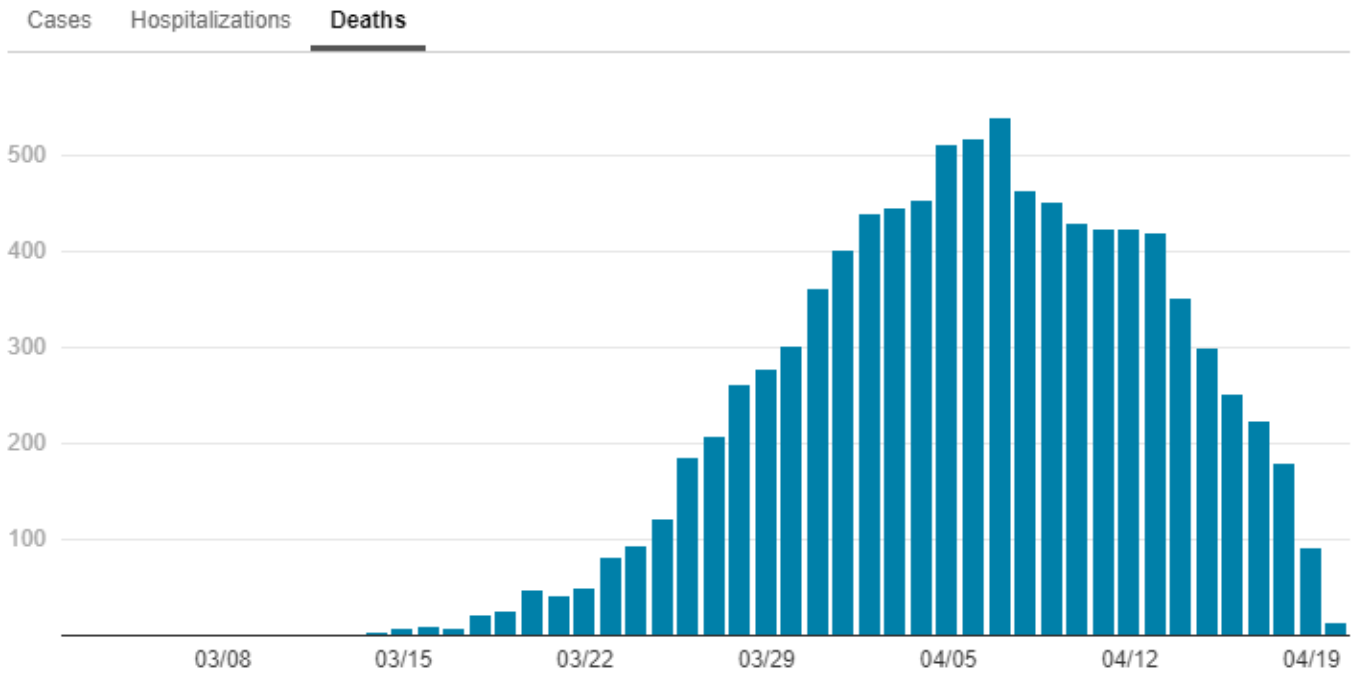
Boston IVF, Waltham, Massachusetts, and Division of Reproductive Endocrinology, Department of Obstetrics, Gynecology and Reproductive Biology, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, Massachusetts

"A large percentage of patients discontinues infertility treatment despite a reasonable prognosis and benefits that cover the costs. Recognition of this problem and appropriate intervention may play a role in helping couples remain in treatment."

Fertil Steril, 2004

The New York Experience

Cases:	**138,435**
Hospitalized*:	**35,920**
Confirmed deaths:	9,944
Probable deaths:	5,052
Updated:	April 22, 2:30 p.m.



Source: https://www1.nyc.gov/site/doh/covid/covid-19-data.page

The New York Experience

Rates by Borough

This chart shows the number of positive cases per 100,000 people in each borough. It indicates the spread of COVID-19 relative to each borough's population.

	Rate per 100,000 people	Count
The Bronx	2,048	30,142
Staten Island	2,026	10,166
Queens	1,655	41,520
Brooklyn	1,318	35,775
Manhattan	911	17,200
Citywide		134,874

Columbia Presbyterian Experience

- March 1st – first confirmed COVID-19 case in New York City
- March 7th – State of Emergency Declared
- March 14th – First confirmed deaths due in New York
- March 18-19 – Two asymptomatic patients admitted for induction of labor developed fever, symptoms
  - Both positive for SARS CoV-2 PCR
  - Required ICU admission
- 15-20 providers exposed without adequate PPE

ELSEVIER

American Journal of Obstetrics & Gynecology MFM

Available online 27 March 2020, 100111

In Press, Journal Pre-proof

COVID-19 Pregnancy Research

COVID-19 in pregnancy: early lessons

Noelle Breslin M.D., Caitlin Baptiste M.D., Russell Miller M.D., Karin Fuchs M.D., Dena Goffman M.D., Cynthia Gyamfi-Bannerman M.D, M.S., Mary D'Alton M.D.

Show more

https://doi.org/10.1016/j.ajogmf.2020.100111 Get rights and content

"Obstetrical care providers are at particularly increased risk for occupational exposure because of long periods of interaction with patients during labor, multiple team members involved in patient care, and the unpredictable occurrence of sudden obstetrical emergencies with their potential for unanticipated intubations in women undergoing labor and delivery."

Hospital Response

- Universal SARS CoV-2 PCR testing of all women presenting to labor & delivery
- Extensive use of PPE – N95 masks for providers, surgical masks for all patients
- Initially, prohibited all visitors including partner/significant other (March 23)
- Change.org petition with hundreds of thousands of signatures protesting this decision
- Governor issues Executive Order allows one support person (March 28)

METRO

Coronavirus in NY: NewYork-Presbyterian hospitals ban women's partners from delivery room

Some Pregnant Women in New York City Will Have to Deliver Babies Alone

"I have not stopped crying," said an expectant mother who learned that her husband could not be with her when she gives birth.

U.S. | NEW YORK

New York Hospital Systems Ban Partners From Delivery Room

NewYork-Presbyterian, Mount Sinai decisions spark backlash from mothers, midwives concerned about heightened risks during labor

'Women Will Not Be Forced to Be Alone When They Are Giving Birth'

In response to some private hospitals' decision to bar partners, New York will order all hospitals to allow partners in delivery rooms, despite the coronavirus risk.

U.S.

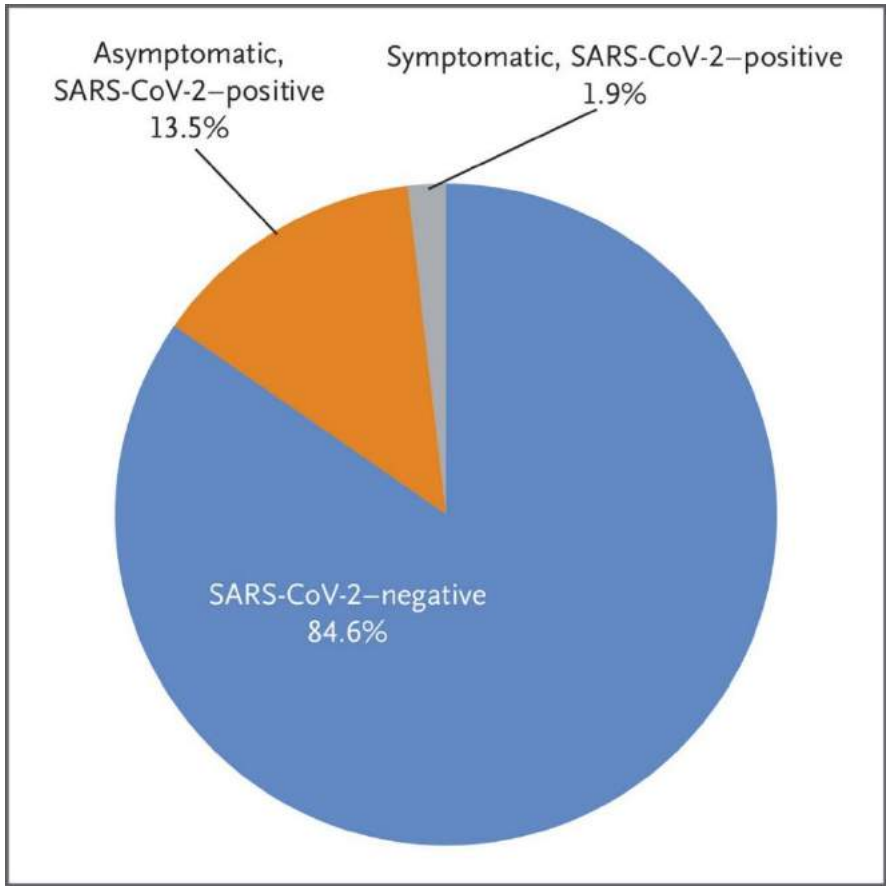
MORE THAN 400,000 PEOPLE SIGN PETITION ASKING HOSPITALS TO ALLOW VISITORS IN DELIVERY ROOMS AMID CORONAVIRUS

Symptom Status and SARS-CoV-2 Test Results among 215 Obstetrical Patients Presenting for Delivery

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

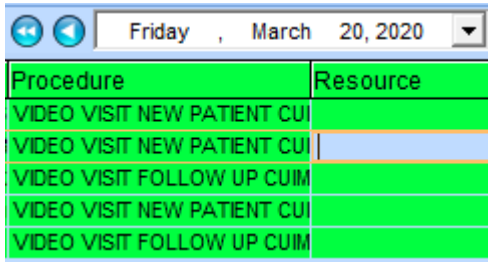
Universal Screening for SARS-CoV-2 in Women Admitted for Delivery



- Between March 22 and April 4- 215 women delivered at the New York–Presbyterian Allen Hospital & Columbia University Irving Medical Center
- All screened for Covid-19 symptoms
- 4 women had symptoms – all positive on SARS CoV-2 PCR
- 210 out of 211 asymptomatic/afebrile women had nasopharyngeal swabs
  - 29 positive on PCR
  - 88% of positives were asymptomatic
- 10% of asymptomatic positives became symptomatic
- 1 initial negative patient became symptomatic postpartum – positive on repeat testing

D Sutton et al. N Engl J Med 2020. DOI: 10.1056/NEJMc2009316

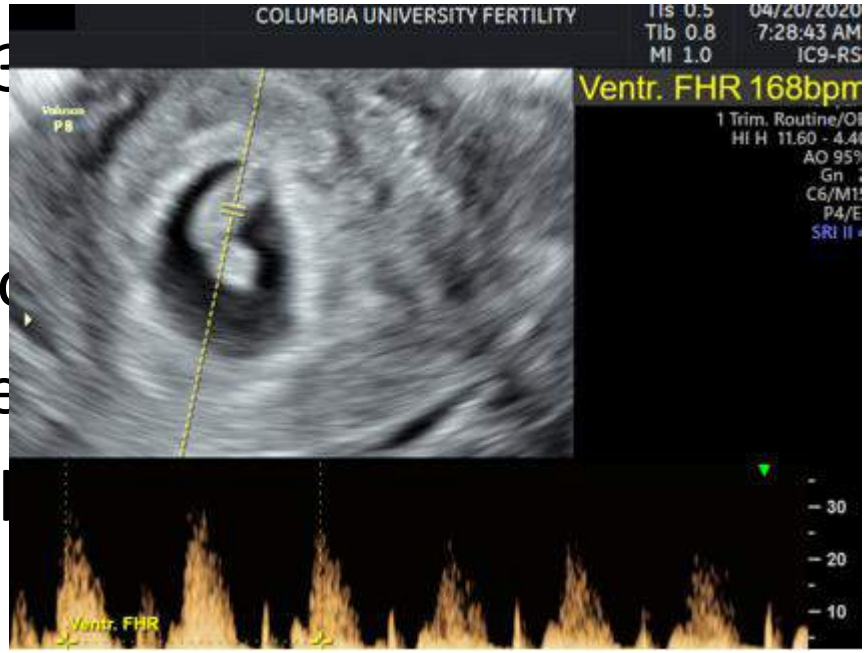
Reproductive Medicine in the Epicenter



- Immediate shift to all telemedicine visits
- Standing Zoom meetings – daily REI division planning call, hospital briefing, OB/GYN Department call
- Shift staff to work from home as much as possible
- Divide critical staff into A/B teams to minimize risk of exposure to entire team
- Provide PPE for staff to travel to and from work

Clinical Vignette 1

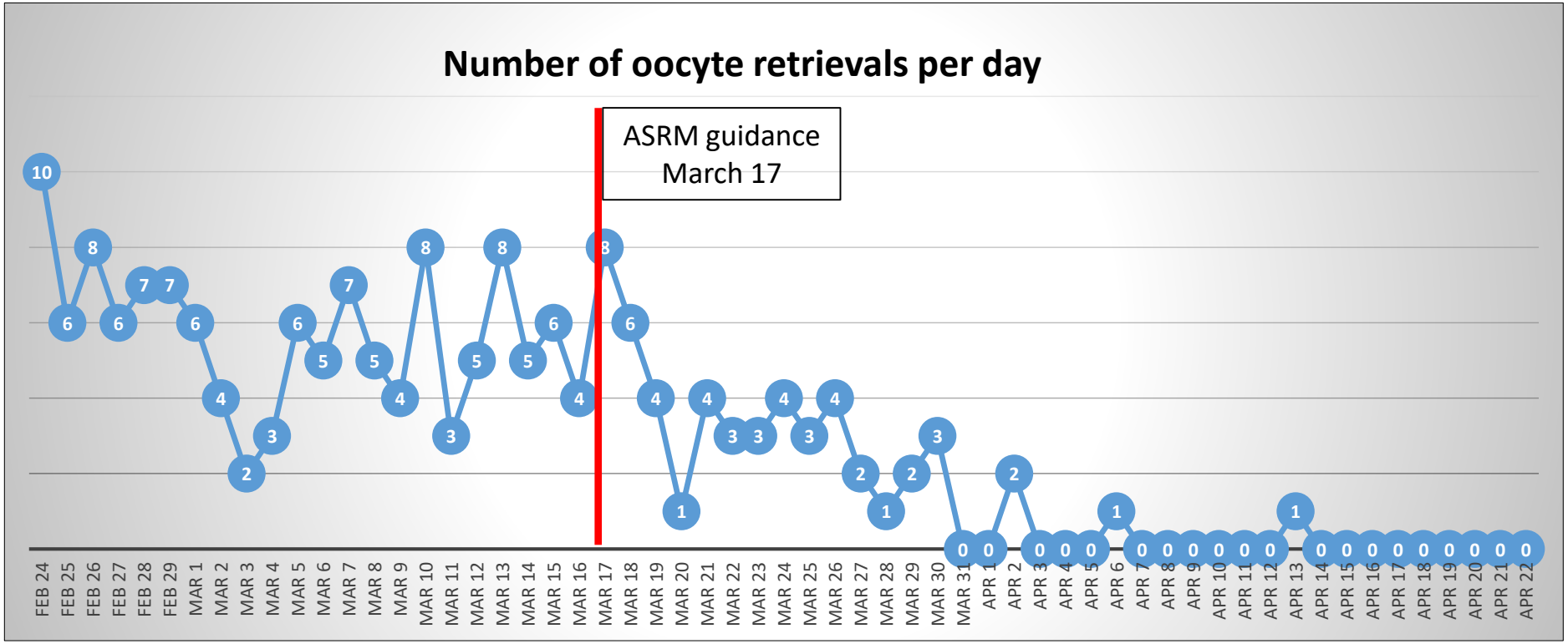
- 28 yo G0 with severe male factor, husband works for NYPD
- Single blastocyst transfer on March 1
- Husband reports Covid exposure and
- March 18 patient and husband test p
- March 22 positive home pregnancy te
- April 6 – Ultrasound confirms IUP wit
  - Symptom and fever free for >7 days
  - PPE worn by staff
- April 20 – Viable 8 week IUP



Clinical Vignette 2

- 35 yo G5P0 with recurrent pregnancy loss planning IVF
- March 17 reports positive home pregnancy test, but has had fever, cough, loss of smell/taste for 5 days
- Vaginal progesterone started empirically – patient advised to follow recommendations of primary doctor and remain home
- After asymptomatic >1 week, ultrasound performed at ~6 weeks by LMP
  - 2 cm ectopic visualized in adnexa, beta HCG > 20,000 mIU/mL
- Due to risk of methotrexate failure, laparoscopy recommended
- Delay of 3 days until Operating Room available
- SARS CoV-2 PCR positive prior to surgery (>2 weeks since symptoms resolved)
- Uncomplicated laparoscopic salpingectomy with extensive PPE

Effect of not initiating new IVF cycles



NEW YORK STATE OF OPPORTUNITY. Department of Health

ANDREW M. CUOMO
Governor

HOWARD A. ZUCKER, M.D., J.D.
Commissioner

SALLY DRESLIN, M.S., R.N.
Executive Deputy Commissioner

DATE: April 7, 2020

Health Advisory: Sexual and Reproductive Health Services During the COVID-19 Public Health Emergency

On March 23, 2020, Governor Cuomo issued an Executive Order 202.10, directing the Commissioner of Health to order all health care facilities, including hospitals and diagnostic and treatment centers, to increase the number of beds available to COVID-19 positive patients. The Executive Order also suspended and modified statutes and regulations, as needed, to accomplish this purpose.

The purpose of this guidance document is to clarify that the **Department considers sexual and reproductive health services as essential services**, however the ultimate decision on when such services must occur is between a patient and clinical provider. These services include but are not limited to:

- Birth control, including Long Active Reversible Contraceptives, such as IUDs;
- Fertility services, including infertility treatment and procedures;
- Gynecological surgeries to address acute complications related to conditions, such as fibroids or endometriosis;
- Abortion services;
- Obstetrical care, such as vaginal and cesarean deliveries;
- Evaluation, diagnosis, and treatment of sexually transmitted diseases;
- Evaluation for cervical and breast cancer, when medically indicated based on patient history and/or physical exam.

Completing fertility evaluation during lockdown

- Options for diagnostic testing are limited as New York State Department of Health has strict rules on diagnostic testing and direct to consumer testing
- At home finger stick testing for ovarian reserve
  - AMH, Estradiol, FSH, LH, Prolactin, TSH, free Thyroxine (Modern Fertility)
- Semen analysis – variety of qualitative tests, Reprosource offers formal report
- Genetic testing - multiple labs provide expanded carrier screening via saliva (SEMA4, Invitae)
  - Report 1-2% no result rate (labels must be filled out correctly)

Modern Fertility

Test your hormones with Modern Fertility

Your clinic is partnering with Modern Fertility to make it easy to test your fertility hormones at home.

Clinic-level results at home
Through this finger-prick blood test, you'll get the same results as a blood draw from a clinic. Your doctor will walk you through your results and recommend next steps.

Personalized fertility reports
Your reports will help you and your doctor discuss how your hormone levels relate to ovarian reserve, egg freezing and IVF outcomes, and other aspects of your reproductive health.

Eligible for HSA or FSA coverage
You can use your FSA or HSA account to purchase the $159 test. Simply download the receipt from your Modern Fertility dashboard and submit the claim online to get reimbursed.

How it works

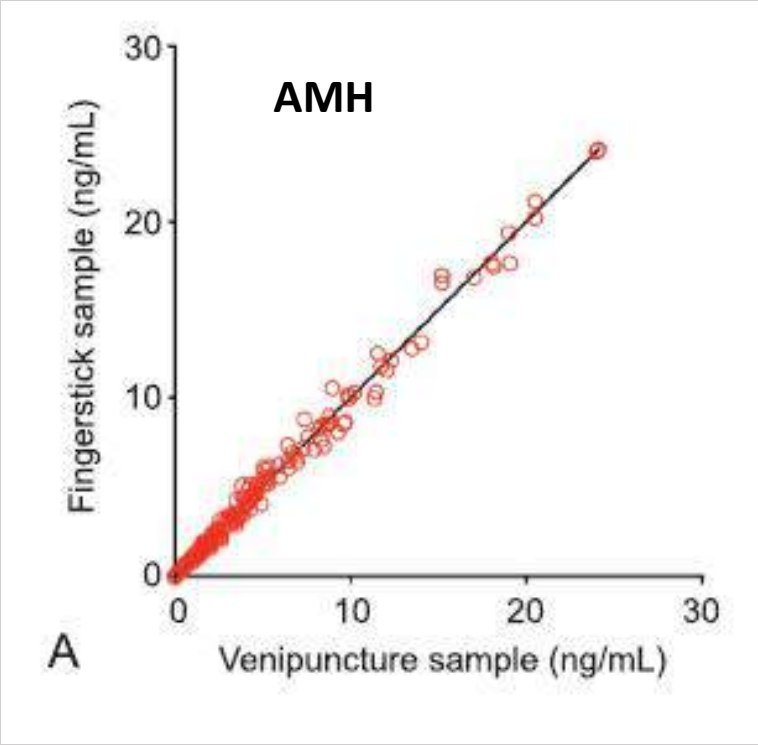
Order your test
Your doctor will provide you with a unique link to purchase the Modern Fertility test online.

Agree to share your results
After you order the test, check the box to give your doctor access to your results and start the conversation.

Take the test and send it in
Send in your completed test using the prepaid envelope. Both you and your clinic will get the results via email, and then your doctor will follow up.

Reproductive Endocrinology and Infertility: *Procedures and Instruments*

Concordance of Fingerstick and Venipuncture Sampling for Fertility Hormones



Semen analysis from home

The ReproSource®
@HOME™
Collection Kit

A Comprehensive Semen Analysis

Collect and ship sample from *home*!

1 ORDER

a. Ask your doctor, or
b. Contact ReproSource

2 COLLECT & SHIP

a. Schedule a FedEx pick up, or
b. Use FedEx drop off location

3 RESULTS

1-2 days

Results sent to your doctor's office in 1 to 2 days

A more physiological sperm collection container?

Introducing
ProteX

Introducing a patented semen collection container that protects sperm from stress during and after collection.

We have revolutionized the semen collection process by creating a collection container designed to reduce the stress on the sperm during collection and protect it until it is processed for use in treatments with ART (Assisted Reproductive Technologies). Our goal is to allow the man to produce the best sample possible for an attempted pregnancy.

Understanding the standard collection process

When the time comes to collect your sample, you will most likely be asked to collect your semen sample by masturbation. Traditionally this is done into a standard, dry specimen cup. This presents some potential challenges to providing the best sample possible, because changes in the environment, especially temperature, very easily damage sperm. Even if the container has been warmed, by the time the sample is collected, the temperature of the container will be cold enough to damage sperm. In addition, the average human semen sample is only about a teaspoon (about 2 ml to 5 ml). When this volume is spread over the bottom of a standard specimen cup, the temperature shifts even more rapidly.

How ProteX can help

ProteX's patented design provides a protective environment for the semen upon collection. The insulated container, funnels the sample into a small holding well to minimize the surface that is exposed to the environment. These features help protect the sample from temperature shifts for a much longer time, which reduces the concern about the time required for collection.

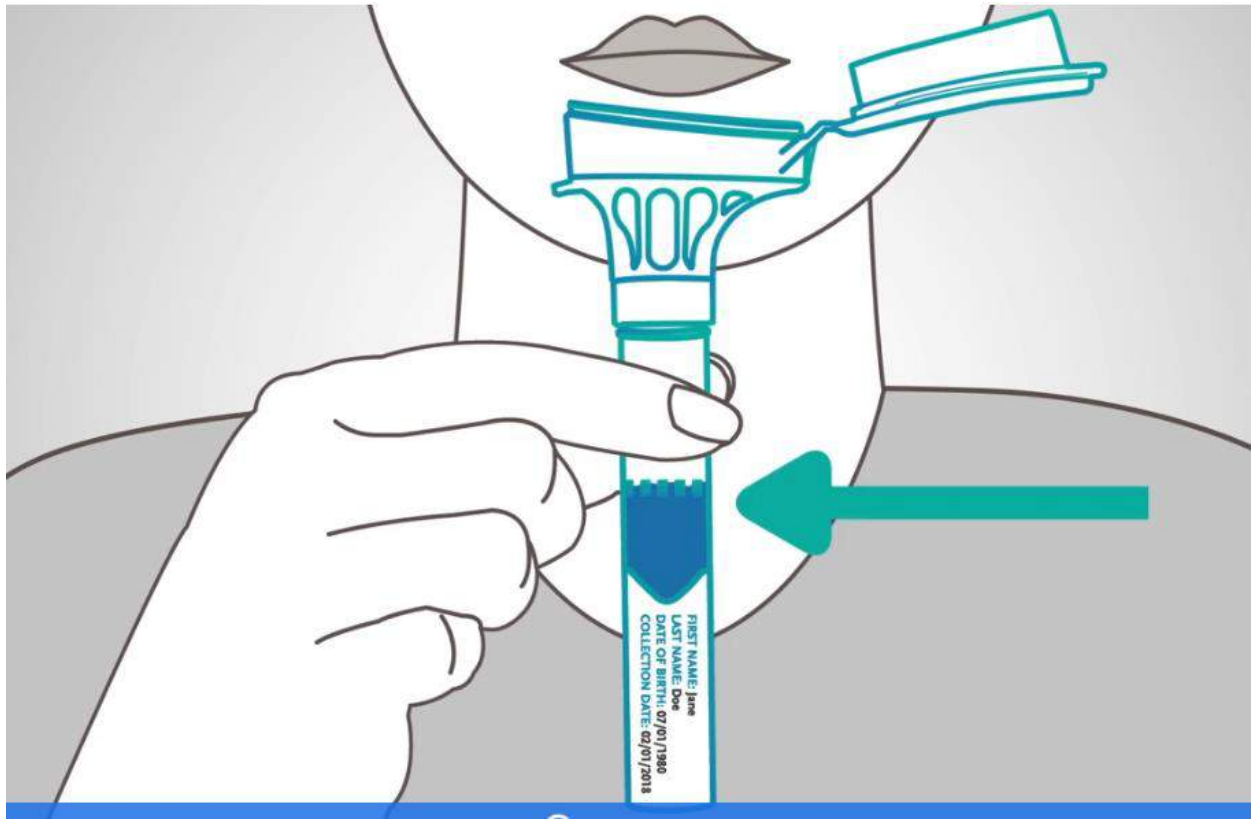
Reduced stress to sperm and patients

In fact, it protects it so well, it gives your fertility team the option of allowing you to collect at home, depending on what they determine is most appropriate for your individual care. Most clinics currently do not allow at home collection with traditional specimen cups because it is almost impossible to maintain the temperature, getting the sample to the clinic in a timely fashion (usually within an hour) and carries a greater risk of having a compromised sample.

Patented design protects samples for damaging temperature changes increasing sperm survival rates

Learn more online at
http://reproductive.solutions

Saliva collection for carrier screening



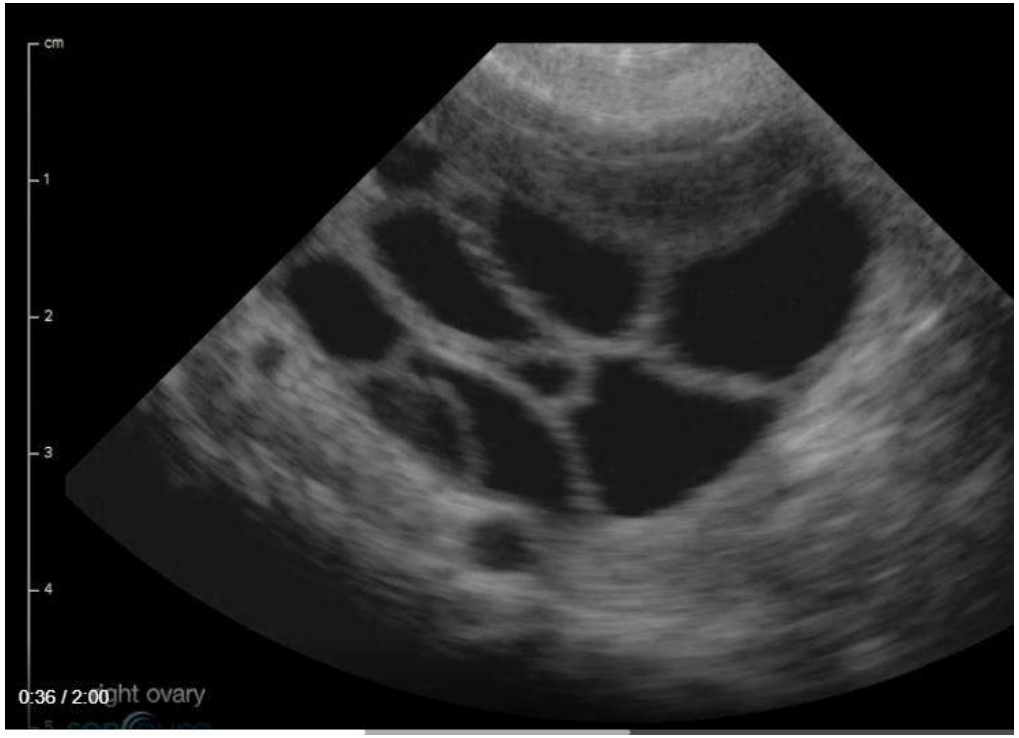
INVITAE

Home Ultrasound

Self-operated endovaginal telemonitoring versus traditional monitoring of ovarian stimulation in assisted reproduction: a prospective RCT

Jan Gerris[1,*], Annick Delvigne[2], Nathalie Dhont[3], Frank Vandekerckhove[1], Bo Madoc[1], Magaly Buyle[1], Julie Neyskens[1], Ellen Deschepper[4], Dirk De Bacquer[4,5], Lore Pil[6], Lieven Annemans[6], Willem Verpoest[7], and Petra De Sutter[1]

- RCT of 121 cycles
- 59 women completed home ultrasound monitoring
- Similar ART outcomes with higher patient satisfaction



http://www.mysonaura.com/docs/Sonaura_end_cycle.mp4

Resuming Treatment

- **Pros**
  - Fertility treatment is time sensitive
  - Infertility is a disease
  - We have passed the peak in the epicenter – hospital admissions, deaths on the decline
  - SARS CoV-2 will be with us for the foreseeable future

- **Concerns**
  - Uncertain impact on pregnancy outcomes
    - No major organizations recommending against pregnancy
    - Pregnancy can be postponed with freeze-all approach
  - Safety of staff
    - Can provide PPE
    - Aim for as close to Covid-free clinics as possible
  - Need to “flatten the curve”
    - Modify protocols to minimize patient visits
    - Maintain physical distance in the clinic

Embryology Laboratory Suggestions For COVID-19 (modified from SART)

- Continue physical inspection of cryostorage tanks, monitoring of liquid nitrogen status daily
- Contact liquid nitrogen supplier - ask for notification if they predict any discontinuity of service
- Gas suppliers may be forced to prioritize
- Stagger embryology staff when possible keep some staff isolated at home
- If needed, train other personnel to be able to monitor, fill tanks
- Obtain extra liquid nitrogen supply cylinders if storage is available
- Continue weekly back-up generator checks
- Complete an inventory of disposable supplies in preparation for resumption of patient care
- Perform preventative maintenance that does not require an outside vendor
- Adjust standing orders for media consistent to perform emergency fertility preservation
- Practical steps in the lab – PPE, cap tubes before discarding, work in isolettes or class II hoods

Is it safe to resume treatment?

- No evidence of SARS CoV-2 in semen from 31 Chinese men with prior documented COVID-19
  - 19% of men had scrotal pain around time of infection
  - ACE2 and TMPRSS2 are sparsely expressed in human testes
    (in press Pan F et al)

- Risk of cross contamination of viruses in liquid nitrogen appears negligible (Pomeroy KO, Fertil Steril 2010; Cobo A, Fertil Steril, 2012)

- Washing of embryos after thaw as well as additional washing with sterile liquid nitrogen further reduces risk (Parmegiani, 2012)

- Possible expression of ACE2 in human embryos
  - Significance unclear

IVF Protocol Modifications

- **Pre-Covid-19**
  - In-person consultation
  - Return visits for screening tests, luteal bloodwork
  - In-person meetings with nurses, coordinators
  - Multiple visits during stimulation – day 1, day 4, day 6, day 8, day 10, post-trigger labs (5-7 visits before egg retrieval)
  - Crowded waiting rooms
  - Rapid turn-over of ultrasound examination room
  - Partner encouraged to accompany patient at visits, egg retrieval and transfer
  - Sperm production in small collection room
  - Signed consent forms – common pens

IVF Protocol Modifications

- **Post-Covid-19**
  - Telemedicine consultations
  - Virtual meetings with nurses, coordinators
  - Consider SARS CoV-2 RT-PCR prior to start of stimulation (if positive, do not start)
  - Temperature checks at each visit (patients and staff)
  - Space out visits during stimulation – day 1, day 5-6, day 8-9, consider post-trigger urine pregnancy test (3-4 visits before egg retrieval)
  - Empty waiting room
  - Thoroughly wipe down surfaces in ultrasound exam room
  - Longer interval between procedures
  - No partners or visitors (encourage use of FaceTime)
  - Off-site sperm production
  - Electronic consent forms – wipe pens if need to sign forms

Conclusions

- The COVID-19 pandemic has had a major impact on New York City and will shape how we practice reproductive medicine in the future
- Telemedicine and physical distancing = new normal
- Fertility clinics must adjust to this new reality to minimize risk to patients and staff
- “Covid-free clinics” may not be possible but we can strive for this goal
- Fertility treatment is urgent and drop out from care is real
  - It can be performed safely and responsibly

Thanks!

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