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00:00:00.000 --> 00:00:03.208 See we are talking.
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00:00:03.210 --> 00:00:07.039 Generally about the topic of uncle fertility,
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00:00:07.040 --> 00:00:11.255 and more specifically about reproductive
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00:00:11.255 --> 00:00:13.784 endocrinology and infertility.
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00:00:13.790 --> 00:00:17.460 Referral for fertility preservation and
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00:00:17.460 --> 00:00:21.003 patients undergoing chemotherapy or Granada.
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00:00:21.003 --> 00:00:27.450 Toxic therapy as as the the the poster said.
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00:00:27.450 --> 00:00:29.676 And we’re joined by two members of
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00:00:29.676 --> 00:00:33.326 the OB GYN department, both who are
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00:00:33.326 --> 00:00:36.386 relatively young in their careers.
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00:00:36.390 --> 00:00:38.609 I don’t actually know who’s going first,
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00:00:38.610 --> 00:00:40.632 and I’m going to introduce both
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00:00:40.632 --> 00:00:42.650 of them together as we start,
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and they can decide that.

So we have two speakers.

We have Tanya Glenn, who's originally from Rochester, and went to college at Truman State University in Missouri and then.

Went on to attend medical school at Saint Louis University School of Medicine.

And took the what is not such a common path of joining the military and did a combined military and civilian residency at at Wright Patterson Air Force Base and Wright University in Dayton, OH.

She's in her final year of REI training at Yale and is going to be taking a position at Brooks Army Medical Center.
After completing her fellowship this year, she is joined by Gabriella Barouch Kim, who is from Los Angeles, originally received her undergraduate degree at UCLA, where she received a number of honors and went on to medical school at UCSF. She is a third year resident in OBGYN and is also interested in REI. And is in the process of applying for reproductive endocrinology fellowships as the parent of a child who went through the Yale OBGYN Residency.
It's always nice to interact with the Yale OBGYN and residents, so they're here today and I'm not entirely sure what order. I'm not entirely sure who's talking but I'm going to leave it to the two of you. You're both on one screen and I think you can figure it out.

Welcome, thank you for joining us. Thank you, thank you for having us. So I'm Gabriella.

I'm here with Doctor Glenn. We're actually going to be co-presenting and Doctor Glenn is going to help answer
questions at the end as well.

OK, your slides. They look perfect.

Perfect thank you so much.

So today as you already mentioned, we’re going to be talking about fertility preservation for patients undergoing gonadal toxic therapy.

Neither Doctor Glenn nor I have any disclosures.

I have any disclosures.

So our objective with this talk is to try to raise awareness for fertility preservation.

Encourage patient and provider discussions surrounding the implications of cancer.

treatment on future reproductive capacity.

improve multidisciplinary collaboration
between providers caring for these patients and reproductive specialists, and discuss options for fertility preservation for patients who hope to preserve their reproductive capacity.

So first I'd like to start with a little bit of background on this topic. The term oncofertility was coined by Doctor Woodruff and it refers to a field of medicine concerned with minimizing the negative effects of cancer treatment on the reproductive system and fertility, with assisting individuals with reproductive impairments resulting from cancer therapy. So what population are we referring to when we discuss fertility preservation?
for patients undergoing cancer therapy?

So over 200,000 people under the age of 49 are diagnosed with cancer annually and 85% of patients less than 39 years old will survive for five years.

70,000 new cases a year of cancer are diagnosed in adolescence and young adults of these patients, more than 90% of them, will survive for at least five years, and these patients tend to be healthier and tolerate more intense therapies, which is relevant because more intense therapies can drastically reduce the reproductive lifespan.
Certain cancer treatments such as radiation, chemotherapy, and surgery, can lead to sterility and subfertility. So next I’d like to briefly discuss what some of the morbidities of these therapies are. Specifically regarding radiation therapy, there are acute morbidities including primary hypogonadism, premature ovarian insufficiency, which was previously referred to as premature ovarian failure, central hypogonadism, specifically for patients who are undergoing radiation to the brain, and then there are late morbidities.
including secondary cancers that can result from radiation therapies, hypothalamic pituitary ovarian access deficiencies. Spinal cord dysfunction, which can potentially lead to impotence among males and infertility or ovarian insufficiency. Regarding the effects of chemotherapy, there are the effects of late morbidity, there are increased risks specifically with people who are premature ovarian insufficiency and primary hypogonadism, and there are increased risks specifically with people who are
receiving alkylating agents or patients with Hodgkin’s lymphoma or breast cancer with undergoing adjuvant therapy where at increased risk of premature ovarian insufficiency. Regarding stem cell therapies and the effects of those, those can lead to gonadal dysfunction and the late morbidity associated with those include secondary cancers and endocrine dysfunction. Lastly, there are the surgical effects of cancer therapies and the acute and long term effects of those include early menopause and sterilization. For example, if somebody would
00:07:08.675 --> 00:07:11.184 need to undergo removal of their ovaries or fallopian tubes.

00:07:15.260 --> 00:07:17.680 So different therapies have different reproductive risks associated with them,

00:07:21.740 --> 00:07:24.205 so high risk therapies include high dose pelvic radiation,

00:07:26.180 --> 00:07:31.780 total body radiation or chemotherapy with high dose alkylating agents,

00:07:34.800 --> 00:07:37.820 whereas low risk therapies include low dose radiation to the pelvis,

00:07:40.000 --> 00:07:45.734 non alkylating chemotherapeutic drugs.

00:07:47.216 Or antimetabolites.
So now I’d like to transition a bit to discuss the importance of counseling these patients. All patients of reproductive age who will undergo potentially gonadal toxic therapies should be receiving fertility counseling. This is in line with guidelines from the American Society of Clinical Oncology, which reports that all oncologic healthcare providers should be prepared to discuss infertility as a potential risk of therapy. The NCCN practice guideline also says that fertility preservation is an essential element of management of
adolescents and young adults with cancer. That being said, less than half of US doctors inform cancer patients of childbearing age about fertility preservation, and only 47% of US doctors routinely refer cancer patients of childbearing age to reproductive endocrinologist. 54% of oncologists do not discuss fertility, according to the JNC that was published in 2013, whereas specifically pediatric oncologists discuss fertility. And what basically this highlights
is that there is a discrepancy between the current guidelines and the reality regarding counseling, and this is something for all of us to work on and an area for improvement to increase access to fertility preservation.

So what about Yale? How are you doing with counseling at Yale regarding fertility preservation for patients undergoing therapy for their cancer? So we do have one study that looks into how what percentage of patients are being counselled specifically for patients who are prescribed cyclophosphamide. The study included 236 reproductive age women between December of 2019 and October of 2021.
And of these 236 patients, 33% received family planning counseling and 9% were offered ovarian tissue cryopreservation. There were certain factors which modified a patient’s likelihood for receiving counseling and those included Caucasian race, age less than 40, and those who had living children were less likely to receive this counseling. So how can we improve access for fertility preservation? There are several things that need to happen for us to achieve that goal.
One is to increase awareness. Next would be to assess patient’s interest in receiving fertility preservation treatment, as well as the provider providing basic counseling regarding fertility preservation. Placing a referral when indicated, and then ensuring that a patient is able to access this care.

So how do we increase awareness? Well, patients are often overwhelmed by a cancer diagnosis, especially when they first receive that diagnosis. They can be worried about delays in cancer treatment,
or they could just be unaware of the potential effects of their therapy on their reproductive capacity.

The medical team already has a considerable amount of counseling to do when a patient receives this diagnosis, and oftentimes that the discussion of fertility preservation cannot be prioritized. However, the onus really falls on the medical team to be able to identify these patients who are at risk and to be able to provide basic counseling and place the referral to reproductive endocrinology when indicated.

So what are some ways that we propose we...
optimize this awareness so one is just through education and collaboration, which is why doctor Glenn and I are here is to try to promote that and something else that we proposed was epic optimization, we proposed was epic optimization, which we’ll talk about a little more in the next slide.

So something that Doctor Glenn and I had proposed to the Epic optimization team is to potentially have a hard stop when a new diagnosis of cancer is entered into a patient’s problem list. A provider could encounter this alert that would require that they acknowledge a reason for either referring a patient
NOTE Confidence: 0.882033265
00:13:12.900 --> 00:13:16.260 to reproductive endocrinology or not.
NOTE Confidence: 0.882033265
00:13:16.260 --> 00:13:18.570 Facing a referral or acknowledging that
NOTE Confidence: 0.882033265
00:13:18.570 --> 00:13:21.238 this is not applicable for this patient.
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00:13:23.850 --> 00:13:27.082 After a after a provider is met with
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00:13:27.082 --> 00:13:29.910 this alert they would then when
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00:13:29.910 --> 00:13:32.802 indicated either place a consult to
gynecology when a patient is in the
NOTE Confidence: 0.860350266333333
00:13:32.802 --> 00:13:36.263 inpatient setting or if they are in
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00:13:36.263 --> 00:13:39.170 simply just place an REI referral.
NOTE Confidence: 0.860350266333333
00:13:39.170 --> 00:13:40.995 the outpatient setting they would
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00:13:40.995 --> 00:13:43.229 simply just place an REI referral.
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00:13:43.230 --> 00:13:46.830 I just want to highlight here that when
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00:13:46.830 --> 00:13:49.682 patients are in the inpatient setting,
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00:13:49.682 --> 00:13:53.280 that console is a general consult to
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00:13:53.280 --> 00:13:56.140 gynecology. Once that console is placed,
NOTE Confidence: 0.860350266333333
00:13:56.140 --> 00:13:58.920 the guide, the inpatient gynecology
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resident team will contact reproductive endocrinology. This can also be done for preservation. For male patients, it would still be a gynecology consult in that case as well. So now regarding education, the Oncofertility Conservatorium was developed in 2007 to address the lack of knowledge concerning fertility, preservation and the National physicians cooperative includes 83 institutions, including oncologists, surgeons, endocrinologists, reproductive endocrinologist, urologist, rheumatologist, geneticist, and mental health providers,
00:14:44.050 --> 00:14:47.770 and below are also different links.

00:14:47.770 --> 00:14:52.066 That can be used by both providers and

00:14:52.066 --> 00:14:56.516 patients to promote education on this topic.

00:15:00.600 --> 00:15:02.216 And then regarding counseling.

00:15:02.216 --> 00:15:04.236 So there are several steps

00:15:04.236 --> 00:15:06.119 involved in counseling patients,

00:15:06.120 --> 00:15:08.848 including informing patients of

00:15:08.848 --> 00:15:12.258 the potential risks to fertility.

00:15:12.260 --> 00:15:13.544 Of their therapy,

00:15:13.544 --> 00:15:16.540 as well as just inquiring whether they

00:15:16.622 --> 00:15:19.297 desire to preserve their fertility.

00:15:19.300 --> 00:15:21.035 Referring patients to REI if

00:15:21.035 --> 00:15:23.190 they are interested as well as

00:15:23.190 --> 00:15:24.945 following up on those patients.

00:15:28.120 --> 00:15:30.290 At this point I want to just
transition a bit to discuss patient perspectives and hopefully this will help highlight again the importance of this topic.

So in a study that looked at female cancer survivors. Umm? There was an increased rate of pregnancy termination among female cancer providers due to a fear of the effect of their therapies on their future children, and what this really highlights is a gap in education.

This study also showed that 91% of female cancer survivors felt that their quality of life was
improved after receiving counseling and treatment about fertility. There was also a cross sectional study concerning fertility after cancer, where the primary outcome was use of fertility treatment and in this study, 75% of participants reported that having a biological child was important to them. 15% of these participants actually used fertility services. And survivors were less likely to pursue infertility treatment due to a fear of adverse effects on their personal health, which again highlights a gap in their education.
Other patient perspectives include a survey from the Journal of Clinical Oncology. In this survey, 81% of teen girls and 93% of their parents would be interested in fertility preservation, even if that method were to be experimental.

In a survey from the Journal of Assisted Reproduction and Genetics, 12.5% of patients reported that they would regret if they were unable to use the tissue that they preserved for ovarian tissue preservation. In these patients and parents felt more in control of their decision with receiving this counseling.

Other patient perspectives.
There are studies and surveys that indicate that 26 to 80% of individuals remember discussing fertility. This range really highlights the variability in each practice. 68% of males and 14% of females remembered being offered a referral for fertility preservation. And then this last statistic reports that female survivors were less likely to be prescribed infertility medications after seeking help, and that relative risk was 0.57. And what this shows us is that there’s also a lack of education among providers.
So next, I’d like to speak about the different methods that can be offered to patients for fertility preservation. There are many proven as well as experimental methods. These include gamete or embryo cryopreservation, ovarian tissue, or whole ovary preservation, suppression of damage which can include decreasing the dose of a certain therapy or using an alternative therapy. Decreasing the dose to the gonads, or steel or shielding the gonads or avoidance of damage entirely.
which could entail. Removing the gonads or using an alternative therapy.

So to discuss some of the proven methods, the gold standard is considered embryo cryopreservation. This process includes stimulating the ovaries with gonadotropins, surgically retrieving oocytes, inseminating the O sites, culturing them for three to five days, and then cryo preserving them. This tends to have a high success with 90% survival of embryos and live birth rates between 22 to 35.
Percent, this whole process takes about two to three weeks, and some of the cons include exposure to high dose hormones, the time involved, and the fact that the patient would need either partner or donor sperm. Another option is mature O site cryopreservation. This tends to have slightly lower success rates between 50 and 90% survival. That’s likely due to attrition of the O sites, as they need to be frozen, thawed, then inseminated. And sorry it fertilized and after fertilization matured.
This process takes essentially the amount the same amount of time as. Embryo choir preservation. There are fewer ethical objections and no partner is required for oversight chair preservation. Another proven method includes O for praxy. This has a success rate between 16 and 90% and involves fixing the ovary to the pelvic brim with a surgical clip. This is typically used for patients who will be exposed to, for example, radiation therapy to the pelvis and what it’s essentially doing is moving.
the gonads away from that site.

There are no ethical obligations, I'm sorry there’s no ethical objections to over prexy and enables a patient to be able to use their own O sites and there’s no stimulation required. Some of the cons include that.

It really depends on a patient’s vascular system. It depends on their age. It depends on the dose of radiation that they’re receiving, and it can also be affected if the area is not shielded. The.

Other methods for fertility preservation,
include ovarian tissue cryopreservation. This was previously thought to be experimental and is now a proven method and involves obtaining ovarian cortical tissue prior to ovarian failure. The tissue is obtained via laparoscopy or laparotomy. The tissue is dissected into small fragments, cryopreserved, and then can later be transplanted. Most typically, that’s done as an orthotopic. Transplant and not a heterotopic transplant. Live birth rates are between 23 to 25% and this is particularly
useful for prepubescent girls, and it can also be used as a form of endogenous hormones.

Once this tissue is retransplantation. Some of the cons include. That reimplantation of potential cancer potential cancer. Once the tissue is removed and then reimplanted the uncertain life span of this tissue. The fact that it requires surgery and may require IVF down the line and the age limit such that patients who are typically over the age of 40 will have less benefit in this case. Next, I'd like to go over just
a few experimental methods which include whole ovary, including pedicle cryopreservation. This is typically reserved for very young patients whose ovaries are very small, for which ovarian tissue, cryo. Location would be very difficult. Another experimental method includes GNRH agonist therapies. The thought process with this is that we shut down the ovaries while a patient is receiving their cancer therapy, and the thought is that when these ovaries are less active, they'll be less susceptible to the
harmful effects of the therapies.

Some alternative options for patients include the use of donor eggs, the use of donor ombria embryos, surrogates or adoption.

Lastly, to go over what happens post treatment for these patients. So regarding evaluation of their fertility down the line, most reproductive endocrinologists or gynecologists would look for patients to resume their menstrual cycle as well as test their anti mullerian hormone level to get a proxy of their ovarian reserve.
and outcomes for these patients, generally we use the same medications. However, as already mentioned, if a patient has an estrogen sensitive cancer, we can consider adding letrozole and aroma taste inhibitor or tamoxifen to reduce the exposure to high levels of estradiol. There are lower pregnancy rates in the first five years with autologous O sites and that lower pregnancy rate is 60%. However, notably, if someone were to use donor O sites,
pregnancy rates tend to be fairly comparable. Regarding pregnancy complications, pregnancy does not affect recurrence of any cancer and generally pregnancy complications tend to be very low. The one exception to this is that some patients who receive very high dose of radiation to the uterus, especially at a young age, can potentially have a bit higher risk. Pregnancy outcomes and pregnancy complications.

Regarding risk to offspring, there is no increased risk of anomalies. However, a provider may consider referring a patient to a genetic
counselor specifically, if there is a genetic predisposition to cancer. Some other concerns that I’d like to briefly discuss include some safety concerns so. It should be determined by a multidisciplinary team, including the medical oncologist and reproductive endocrinologist. As to a discussion of the risks, benefits, preferences, and prognosis of this patient to discuss whether pursuing fertility preservation would be safe for the patient.
There should also be consideration paid to trying to prevent any delays in oncologic treatment. Regarding the legal implications, we should acknowledge the legal implications of not following the standard of care as well as the medical liability and potential malpractice with omission of information specifically regarding the risks of cancer therapies on reproductive capacity. Additionally, the ethical considerations to consider that every patient has the right to know their options concerning fertility preservation as well as the risks and costs associated with that.
Posthumous utilization. This typically will depend on a patient’s advance directive. Minors who are diagnosed with cancer will typically require a surrogate decision maker. And of course, the cost of these therapies. Just to briefly discuss the cost. There is legislation regarding costs specifically in Connecticut. In general, in 1942, the US Supreme Court acknowledged that procreation is a basic civil right and then specifically in Connecticut.
We do have the fertility preservation bill. This was an acted, basically it ensures that patients are covered for fertility preservation. If they have a medical necessity and having prior cancer treatment is considered, makes fertility preservation a medical necessity, and so patients who have private insurance. Have have this cost covered under this bill. Unfortunately, that bill does not cover the cost for people without insurance or for people with Medicaid, and so there are other means to try to reduce that cost for those patients,
and they are listed below.

So for example, with repro tech, they provide discounted long term storage of ovarian tissue as well as O sites and embryos, specifically regarding the cost of ovarian tissue prior preservation that one tends to be a bit costly. And can be between 12 to 24,000. However, this can also vary based off of the patient’s income. And so lastly, to summarize, some of the things that we discussed today.
Certain cancer treatments such as chemotherapy, radiation and surgery can lead to sterility and subfertility all patients of reproductive age who will undergo potentially genotoxic therapies should receive appropriate counseling. Some of the methods to try to optimize access to fertility preservation include increasing awareness, promoting education and counseling, and collaboration, and methods. To preserve fertility, include embryo 4 O site cryopreservation, ovarian tissue cryopreservation, or experimental methods.
Thank you so much for your attention. Here are some of our references and we're happy to answer any questions.

There's.

OK, so we have a question here regarding oh for proxy. The range of success rates listed are quite wide, from 10 to 90%.

I had heard roughly a 50% chance of damaging the ovary directly from the procedure itself, which seems a high risk since since the risk from radiation is also probabilistic. Does Yale offer this option? What do the success rates look like?
in modern practice and what patients?

Do well versus poorly with this approach.

I actually have not seen any perplexity done here at Yale, but it is actually a simple procedure.

It’s the same thing.

If we had some with ovarian torsion, it’s actually the same procedure to be done, so it’s something that we can actually do.

I haven’t seen a whole lot of public radiation patients come through. I couldn’t give you the exact statistics, mainly because the problem is like it varies on dose. Where it’s located?

Are they shielding or not?
And so that’s why you see that wide range.

So even with Uber, Paxi would probably still recommend doing an additional. Fertility preservation procedure like tissue or embryo cryopreservation. Just to make sure that if there is any scatter from the radiation we’re still protecting them as much as possible.

So I have a question for you, obviously these issues come up with a fair amount of frequency, and I’m struck that you gave a great talk, but one of you is going off to take
a job in Texas and Gabriella,

you're going off to do a fellowship in another year.

So who on the REI? Faculty is interested in these issues,

who we should approach?

Well, Gavin, be here for another year and so I understand that. But you know,

again. So in training no, absolutely. And so we're working with Doctor Callan as well,

and she does mainly the probably the most of the fertility preservation.

But the fellows all work together too,
kind of passed down for.

So my second year fellow, who’s a rising third year now Eric Kahn, would be another good point. Of reference as well.

There’s another chat. The questions. Can you talk a little bit more about your outpatient services? How quickly can these patients be seen, particularly those who need to start anti cancer treatment quickly?

Absolutely. So usually the third year fellow actually does all of the Medicaid referrals and other referrals as well.
00:33:36.960 --> 00:33:38.016 If you just mark them urgent,
NOTE Confidence: 0.77724546125
00:33:38.020 --> 00:33:39.628 we usually can see them within
NOTE Confidence: 0.77724546125
00:33:39.628 --> 00:33:41.800 a week if not faster inpatient.
NOTE Confidence: 0.77724546125
00:33:41.800 --> 00:33:44.194 Of course we see within 24 hours a lot
NOTE Confidence: 0.77724546125
00:33:44.194 --> 00:33:46.388 of times it’s just be like video chat
NOTE Confidence: 0.77724546125
00:33:46.388 --> 00:33:48.380 so we can just talk about the options.
NOTE Confidence: 0.77724546125
00:33:48.380 --> 00:33:50.702 And start getting things set up on our end,
NOTE Confidence: 0.77724546125
00:33:50.710 --> 00:33:52.786 but usually we see people very
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00:33:52.786 --> 00:33:55.339 quickly and you know we manage to
NOTE Confidence: 0.77724546125
00:33:55.339 --> 00:33:57.169 squeeze them in somewhere because
NOTE Confidence: 0.77724546125
00:33:57.169 --> 00:33:59.740 we know how important this is and.
NOTE Confidence: 0.77724546125
00:33:59.740 --> 00:34:03.116 You know the hard part is when patients
NOTE Confidence: 0.77724546125
00:34:03.120 --> 00:34:04.626 you know are not stable enough,
NOTE Confidence: 0.77724546125
00:34:04.630 --> 00:34:06.114 and those are probably the hardest patients,
NOTE Confidence: 0.77724546125
00:34:06.120 --> 00:34:08.815 and so usually if they have to
NOTE Confidence: 0.77724546125
00:34:08.815 --> 00:34:10.880 undergo cancer treatment immediately,
we want to make sure that they know how to find us afterwards so we can start planning after their treatment as well.

Ohh Kurt, is there any movement to extend reproductive coverage to patients with Medicaid? I wish I’ve not seen any movement from. Fortunately for that, I think there’s this an ongoing struggle. The hard part too is. I’m not originally from East Coast, but since all the states are so small each time you move states we see a lot of patients from Rhode Island and Massachusetts and New York and all of
those states have different policies when it comes to fertility preservation, and so it makes it very difficult to keep up with. I think, but I have not seen any improvement in that area. Can you clarify if the quality statistic is independent of whether or not the patient used preservation strategies? I think the stress is the importance of referral, regardless of whether or not you have time. Yes, it does. Patients, even if they cannot pursue the treatment.
 Especially they can’t pursue it immediately.

Still appreciate the counseling that they receive so that they’re aware of it.

It’s not 10 years down the road that they’re surprised by this outcome.

Something as well as that we’re doing a lot more ovarian tissue crime preservation.

I’m doctor ate. Who’s a Yale physician, but recently has been working a little bit more with us.

we’re doing a lot more ovarian tissue crime preservation.

He does the ovarian tissue crime

preservation, he kind of based out of New York when he comes down and does ovarian just require preservation,
and does a lot of research on fertility, preservation, and so we're lucky to have him and that we can kind of continue. Still other areas that we're trying to improve on is, you know, testicular tissue prior preservation. Hopefully we will get more. That does that for prepubescent boys, I think in Philadelphia or Pittsburgh around here. That does that for prepubescent boys, that is still experimental, but there's a lot of different things that we're just trying to bring more to Yale so that we can ensure that we kind of cover...
everyone for fertility preservation.

When it comes to male fertility preservation. It's usually if they're postural, very straightforward. If there's any problem with **********

or the patients are unable to do so, we just have our colleague from Urology, Dr. Honig, help us with that, but we have our own andrology lab and store sperm here.

Any other questions? Well, thank you both. It was really great and we look forward to interacting with your colleagues in the in

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the years ahead and good luck.