Fertility & Assisted Reproduction for Previvors

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Disclosures

No conflicts to disclose
Hereditary Cancer Syndromes

• Majority of women with inherited breast and/or ovarian cancers carry a deleterious mutation for either $BRCA1$ or $BRCA2$. 
Less Commonly, Cancer is Due to Other Hereditary Syndromes

<table>
<thead>
<tr>
<th>Hereditary Cancer Syndromes</th>
<th>Cancer Risk</th>
<th>Hallmarks</th>
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<tbody>
<tr>
<td><strong>Lynch</strong>, also known as hereditary nonpolyposis colon cancer (HNPCC)</td>
<td>Colon, endometrial, ovarian &amp; stomach</td>
<td>Gastrointestinal polyps</td>
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<tr>
<td>Li-Fraumeni</td>
<td>Breast, sarcomas, brain, leukemia, &amp; adrenocortical</td>
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<tr>
<td>Peutz-Jeghers</td>
<td>Gastrointestinal, breast &amp; ovarian</td>
<td>Benign skin lesions &amp; gastrointestinal polyps</td>
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<td>Cowden</td>
<td>Breast, endometrial &amp; thyroid</td>
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<tr>
<td>Hereditary diffuse gastric cancer (HDGC)</td>
<td>Gastric &amp; lobular breast</td>
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Newer Cancer Genetic Screening Panels

- Sema4
  - CancerNext panel
    - **34-gene panel** that identifies inherited risks for at least 8 types of cancers.
      - APC, **ATM**, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, DICER1, EPCAM, GREM1, HOXB13, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, NF1, **PALB2**, PMS2, POLD1, POLE, PTEN, RAD50, RAD51C, RAD51D, SMAD4, SMARCA4, STK11, TP53.
  - CancerNext-Expanded
    - Next-generation sequencing panel analyzing **67 genes** associated with increased risks for brain, breast, colon, ovarian, pancreatic, prostate, renal, uterine, and many other cancers.
      - AIP, ALK, APC, **ATM**, BAP1, BARD1, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN1B, CDKN2A, CHEK2, DICER1, EPCAM, FANCC, FH, FLCN, GALNT12, GREM1, HOXB13, MAX, MEN1, MET, MITF, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, NF1, NF2, **PALB2**, PHOX2B, PMS2, POLD1, POLE, POT1, PRKAR1A, PTCH1, PTEN, RAD50, RAD51C, RAD51D, RB1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, SMARCB1, SMARCE1, STK11, SUFU, TMEM127, TP53, TSC1, TSC2, VHL, XRCC2.
BRCA: Background

• Prevalence of BRCA:
  - In an unselected non-Jewish population in the U.S., the chance of having a BRCA mutation is 1 in 400*.
  - In Ashkenazi Jews, approximately 1 in 40 individuals has a BRCA mutation.**

• Patients with a BRCA mutation are at increased risk of breast, ovarian, as well as other cancers, with an earlier age of onset***.

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<tr>
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<th>Lifetime Breast Cancer Risk</th>
<th>Lifetime Ovarian Cancer Risk</th>
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<tbody>
<tr>
<td>BRCA 1</td>
<td>50-85%</td>
<td>50-85%</td>
</tr>
<tr>
<td>BRCA 2</td>
<td>40-60%</td>
<td>16-27%</td>
</tr>
<tr>
<td>General Population</td>
<td>13%</td>
<td>1.4%</td>
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Oncofertility

A delay in childbearing combined with an improvement in cancer survival rates have resulted in more and more women having not had children at the time of their cancer diagnosis and requiring fertility preservation.

As a result, “Oncofertility” is now a discipline:
- Interdisciplinary field at the intersection of oncology and reproductive medicine that expands fertility options for cancer survivors.
- Significant proportion of young women diagnosed with cancer are given the opportunity to preserve their fertility before undergoing gonadotoxic treatment.
Chemotherapy Can Be Harmful to Ovaries

The degree of damage is dependent on a few factors:

• The most important of these factors is the type of chemotherapy.
  - High risk for inducing ovarian failure:
    • Cyclophosphamide (alkylating agent) often used to treat early stage breast cancer.

• Dose dependent

• Age Dependent
  - Older patients who have less ovarian reserve are at highest risk for ovarian failure.
    • In women with breast cancer treated with chemotherapy, more than 50% of 40+ year olds experienced ovarian failure versus 30% in those 35 or less.

The loss of ovarian function may be permanent or temporary with temporary amenorrhea (no menses).

There is no data to suggest that chemotherapy directly damages the uterus.
Reproductive Success After Cancer and Treatments is Substantially Decreased

- Patients who have undergone cancer treatment without fertility preservation have a substantial decrease in their fertility.
  - Childhood Cancer Survivor Studies demonstrate that female survivors were substantially less likely to have live births compared with their siblings.
  - Among female cancer survivors that did not use fertility preservation, there appears to be an increase in the use of IVF and a significant decrease in first-time parenthood probability.

- Utility of outcome data in several studies assessing ovarian function after cancer treatment is often limited and does not tell the entire story because menses rather than pregnancy is used as an endpoint.
  - Menses ≠ ability to conceive.
Current Best Approach to Fertility Preservation is Egg or Embryo Freezing

- Ovarian stimulation for embryo cryopreservation or mature oocyte cryopreservation (egg freezing) is the current best method to preserve reproductive potential in women of reproductive age and remains the most likely strategy to result in a subsequent pregnancy in women diagnosed with cancer.
  - Cryopreservation refers to the cooling of cells and tissues to sub-zero temperatures in order to stop all biologic activity and preserve them for future use.
BRCA and Risk-Reducing Bilateral Salpingo-Oophorectomy (BSO)

- Women with a BRCA mutation may consider a prophylactic salpingo-oophorectomy (excision of fallopian tubes and ovaries) to decrease cancer risk.

- Guidelines recommend risk-reducing bilateral salpingo-oophorectomy (BSO) between the ages of 35-40, or individualized based on age of onset of ovarian cancer in a family member and once childbearing is complete.
  - Studies show that BSO significantly reduces the risk of ovarian cancer.
  - Alternative risk reducing strategy
    - Risk reducing salpingectomy followed by delayed oophorectomy.
    - Growing evidence that fallopian tube is origin of ovarian cancer.
    - However, data on its effects on ovarian cancer risk are lacking.

- Various medical interventions to reduce cancer risk or treat malignancy often elicit fertility and family-planning concerns among young BRCA mutation carriers.

- Specific recommendations for breast cancer risk management include intensive screening as well as consideration of hormonal and surgical forms of risk reduction.
  - In addition to bilateral mastectomy in premenopausal women, obtaining BSO by the recommended age may significantly reduce risk of breast cancer.
Children of BRCA Mutation Carriers Have a 50% Chance of Inheritance

• Option of IVF with preimplantation genetic testing for monogenic/single gene defects, currently referred to as PGT-M (formerly known as PGD- preimplantation genetic diagnosis) to screen out the mutation.
Does Being a BRCA Carrier Impact Fertility?

• Conflicting studies exist regarding effect of a BRCA mutation on fertility.

• There are multiple studies suggesting BRCA mutation carriers (more BRCA 1 compared to BRCA 2) may have decreased ovarian reserve (lower egg quality and quantity) compared with women without BRCA mutations, as well as onset of natural menopause at an earlier age. Some studies have also implied that BRCA mutation carriers undergoing in vitro fertilization (IVF) may not do as well compared to non-BRCA carriers.*

• However, some studies failed to demonstrate an association between BRCA status and fertility.**

Circulating AMH is a biomarker of ovarian reserve.

Findings:
- BRCA1 mutation carriers had a 25% lower AMH concentrations than non-carriers and were more likely to have AMH concentrations in the lowest quartile for age.
Antimüllerian hormone levels are lower in BRCA2 mutation carriers

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Objective: To compare antimüllerian hormone (AMH) levels in women at high risk for hereditary breast and ovarian cancer compared with healthy low-risk control women.

Design: Prospective cohort.

Setting: Not applicable.

Patient(s): Reproductive-age women with a uterus and both ovaries were analyzed in four groups: BRCA1 mutation carriers, BRCA2 carriers, BRCA-negative women, and low-risk controls.

Intervention(s): Self-collected dried blood spot.

Main Outcome Measure(s): AMH levels.

Result(s): One hundred ninety-five women were included: 55 BRCA1 carriers, 50 BRCA2 carriers, 26 BRCA-negative women, and 64 low-risk controls. After adjusting for confounders, BRCA2 carriers had AMH levels that were 33% lower than control women and an increased odds of having AMH < 1 ng/mL. BRCA1 carriers and BRCA-negative women had AMH levels similar to control women. When analysis was restricted to regularly menstruating women younger than 40 years of age, BRCA2 carriers continued to demonstrate significantly lower AMH levels and increased likelihood of low AMH. Also, in this restricted group, BRCA-negative women demonstrated AMH levels that were 42% lower than control women. No difference in AMH was observed for BRCA1 carriers.

Conclusion(s): We observed significantly lower AMH levels among BRCA2 carriers compared with low-risk control women. These results were stable across all models. BRCA-negative women also had lower AMH values, but only in models restricted to young regularly menstruating women. In contrast to earlier analyses, BRCA1 carriers had AMH values that were similar to low-risk control women, but this may be due to differences in the population studied. (Fertil Steril® 2017;107:1256-65. ©2017 by American Society for Reproductive Medicine.)

Key Words: BRCA, antimüllerian hormone, ovarian reserve, fertility

Discuss: You can discuss this article with its authors and with other ASRM members at https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/15485-23461
Abstract presented at the ASRM annual conference October 2016

Findings:
- A trend toward accelerated age-related decline in ovarian reserve and oocyte yield was demonstrated in BRCA 1 carriers.
- Although patients who carry the BRCA mutation are known to have altered DNA repair mechanism, their embryos did not demonstrate an increased rate of aneuploidy (chromosomally abnormal embryos), although the number of patients was small in this study.
Women who express a BRCA mutation have been shown to accumulate damaged DNA, which may stimulate the aging of eggs and their depletion.

Findings: Despite the subtle decrease in ovarian reserve and trend towards reduced blastulation rate seen in BRCA carriers, embryo quality was not affected.
What Factors Influence BRCA Carriers’ Decisions on Trying to Conceive?

- BRCA carriers are faced with difficult issues regarding their desire to conceive:
  - Risk-reducing surgery (bilateral salpingo-oophorectomy {BSO}).
    - When?
  - Potential risk of diminished ovarian reserve.
  - Risk for passing on the mutation to their offspring.
    - 50% of offspring will be a carrier.

- Other factors that may influence BRCA carriers’ decisions on trying to conceive:
  - Age
  - Single vs. married
  - Size of family desired
I am a BRCA Carrier and Want to Have Children in The Future, What Are My Options?

• Oocyte cryopreservation (egg freezing).
  - Single/Not in a Committed Relationship.
    • Considering risk-reducing BSO in near future.
    • Diminished ovarian reserve.
  - In future, after thaw and fertilize eggs, can biopsy developing embryo and undergo PGT-M (formerly known as PGD).

• Embryo cryopreservation (embryo freezing).
  - Married/In a Committed Relationship.
    • Considering risk reducing BSO in near future prior to completing their family.
    • Diminished ovarian reserve.
  - Option of PGT-M.

• Annual monitoring of ovarian reserve (AMH and follicle scan of ovary) given possible increase risk of diminished ovarian reserve.

• PGT-M

• No fertility-related treatment or monitoring.
What Does an IVF/Egg Freeze Cycle Involve?

There are several steps in an IVF cycle:

- Ovarian Stimulation and Monitoring
- Egg Retrieval
- Fertilization and Embryo Culture
- Embryo Transfer
What Does an IVF/Egg Freeze Cycle Involve?

Ovarian Stimulation and Monitoring

• A patient undergoing IVF usually takes hormone injections for 8-12 days to increase the number of eggs. Frequent monitoring (bloodwork and ultrasound) is performed to follow the ovarian response, allowing medication dosage adjustment.
What Does an IVF/Egg Freeze Cycle Involve?

Egg Retrieval

• Under sedation, a fertility specialist extracts eggs via ultrasound guidance. The egg retrieval is a minimally invasive procedure that normally takes less than 15 minutes.
  - In an egg freeze cycle, the eggs are frozen on the same day.
What Does an IVF/Egg Freeze Cycle Involve?

Fertilization and Embryo Culture

- Embryologists use high-power microscopes to fertilize the eggs with sperm in the embryology laboratory. The resulting embryos are then cultured in a dish.
What Does an IVF/Egg Freeze Cycle Involve?

Embryo Transfer

• A fertility specialist uses an abdominal ultrasound to guide a small catheter through the cervix and place the embryo(s) in the uterus. This procedure usually does not involve any sedation and takes only a few minutes.
Egg Freezing

• Early results from egg freezing were disappointing:
  - Low egg survival, fertilization and pregnancy rates after IVF with thawed eggs.
  - Initial protocols used a slow freeze and rapid thaw.
  - Mature eggs are difficult to freeze because of the meiotic spindle and formation of ice crystals.

• New Protocols
  - Modifications in cryoprotectant solutions.
  - Vitrification: process of cryopreservation using high initial concentrations of cryoprotectant and ultra-rapid cooling to solidify the cell into a glass-like state without the formation of ice crystals.
Vitrification is Superior to Slow Freezing

- Multiple studies demonstrated superior results after vitrification.
  - Higher egg survival rate.
  - Higher fertilization rate.
  - Higher top-quality embryos and cleavage rate.
  - Greater clinical pregnancy rate per thawed/warmed egg.

- Vitrified eggs have success rates comparable to fresh eggs.
  - Comparable fertilization rates, embryogenesis and pregnancy between vitrified eggs and fresh eggs.

- In fact, in 2012 ASRM revised their committee opinion and stated that this is no longer experimental and currently vitrification is the preferred method of cryopreservation. From the published ARSM opinion:
  - Good evidence that fertilization and pregnancy rates are similar to IVF/ICSI with fresh eggs.
  - No increase in chromosomal abnormalities, birth defects or developmental deficits in the offspring.
  - Evidence indicates that oocyte vitrification (egg freezing) and warming should no longer be considered experimental.
How Many Eggs Do I Need?

- A frequent question when discussing egg freezing with patients is the number of eggs required to maximize their chances of success in the future.
  - Everyone is so different that there is a wide range based on one’s egg quality.
  - Best approach is based on chronologic age and chromosomal content.

- How many eggs does it take to make a baby?
  - 1 egg ≠ baby

- Ideal number varies based on the patient’s age, desired family size and finances.
  - No right or wrong answer
  - 10-20 mature eggs is typically the goal
  - Recent abstract by Goldman presented at ASRM 2015 looked at the number of mature eggs to achieve a live birth.
    - < 35: 8 eggs
    - 35-37: 10 eggs
    - 38-40: 14 eggs
PGT-M

- Preimplantation genetic testing for monogenic/single gene defects (PGT-M), formerly known as preimplantation genetic diagnosis (PGD), is the diagnosis of a genetic condition prior to achievement of a pregnancy.
  - Identifies embryos that are predicted to be affected with a genetic disease and those that are not, therefore allowing couples to prevent a pregnancy with a genetic condition.
  - PGT-M is the only way to determine whether an embryo is predicted to be affected with a genetic condition prior to achieving pregnancy.

- Requires blood work from the patient and the partner in order to create a “DNA probe” for the specific genetic mutation.
  - Depending on the genetic disorder, a buccal (cheek) swab from other family members (i.e. parents) may also be requested.
  - Usually takes 4-8 weeks to create the specific probe.

- An IVF cycle involving PGT-M includes the process of fertilization of the egg, culture of the embryo to the blastocyst stage, embryo biopsy, embryo freezing by vitrification, and DNA analysis to determine if the embryo carries the mutation for the specific disease (such as BRCA).
Aneuploid Screening and PGT-M

• Aneuploid screening allows for assessment of chromosomal abnormalities in the embryo (i.e. down syndrome, turner syndrome, trisomies, etc.).
  - Aneuploidy (a chromosomally abnormal embryo) is the leading cause of implantation failure and miscarriage after IVF using unscreened embryos.*
  - Aneuploidy increases with increasing maternal age which is why older women have lower pregnancy rates and higher miscarriage rates in an IVF cycle using unscreened embryos.

• In almost all PGT-M cycles, embryos also undergo preimplantation genetic testing for aneuploidy (PGT-A), formerly known as preimplantation genetic screening (PGS), or comprehensive chromosomal screening (CCS).

• This process allows us to identify the single healthiest embryo that is unaffected with the BRCA mutation and chromosomally normal (euploid). These embryos are later thawed and transferred in a frozen embryo transfer cycle (FET).

• Excess euploid and unaffected BRCA embryos can be saved for future attempts at pregnancy, since these embryos can remain frozen indefinitely.

*Scott 2012, Nasseri 1999, Wener 2012
Embryo Biopsy at the Blastocyst Stage
The purpose of this study was to assess the informational needs of BRCA mutation carriers regarding issues of fertility and preimplantation genetic diagnosis options. 13 women participated in a focus group at the 2009 Facing Our Risk of Cancer Empowered (FORCE) national conference.

- Eligible participants included:
  - Carrier for BRCA mutation.
  - Strong family history of breast or ovarian cancer.
  - Personal history of breast or ovarian cancer.

Women with a BRCA mutation have unique concerns about childbearing and future fertility. In a focus group conducted among unaffected carriers, the majority of women held positive attitudes toward preimplantation genetic diagnosis to reduce transmission to future offspring and further identified unmet needs for education and support for decision making. (Fertil Steril® 2010;94:2473–5. ©2010 by American Society for Reproductive Medicine.)
Findings Highlighted by the Focus Group

- The results of this study highlighted the important psychosocial concerns and informational needs within this population.
  - Explored the informational needs of women who were BRCA carriers regarding issues of reproduction and views on PGD.
  - The study demonstrated that BRCA carriers have “special informational needs regarding issues of cancer prevention, *fertility options*, as well as the need for psychosocial support from health care professionals.”
  - Participants believed information about fertility options and PGD was not well discussed by health care providers.
Findings Highlighted by the Focus Group

- Feelings of guilt about transmitting the mutation to future children existed.
- Limited quantity of information about fertility options was disappointing.
- Most felt a sense of responsibility to take advantage of PGT-M technology but thought a lack of information about the process and procedures existed.
- The majority agreed that even if IVF and PGT-M were not pursued, there was an implied responsibility to at least consider options.
- A strong desire for assistance with decision making.
  - “A need for a new era of family health professional and preferred to receive PGD information in an organized and systematic manner from a professional devoted to working solely with BRCA mutation carriers.”
Recent Abstracts Presented at ASRM

• BRCA MUTATION CARRIERS: A NEW TARGET POPULATION FOR FERTILITY PRESERVATION CONSULTATION AND TREATMENT (Kim 2013)
  - Findings:
    • Most women with BRCA mutations were interested in fertility preservation consultation/treatment if they had not yet completed childbearing at time of screening.
    • This well-educated group had limited knowledge about the clinical impact of a risk-reducing BSO on subsequent fertility, or the benefit of a fertility preservation consultation with egg/embryo banking before a risk-reducing BSO.
    • BRCA-positive women tended to report difficulties in conceiving.
    • Targeted referrals for fertility preservation consultation at the time of BRCA screening may help women improve knowledge and allow improved decision-making about reproductive options.

• REPRODUCTIVE DECISION-MAKING IN PATIENTS DIAGNOSED WITH BRCA MUTATIONS (Chan 2015)
  - Findings:
    • The knowledge of BRCA carrier status impacts behaviors regarding marriage and childbearing and the majority of BRCA carriers believe that PGD and prenatal diagnosis should be offered.
    • BRCA carriers desire and would benefit from reproductive counseling after being informed of their carrier status.
The purpose of the study was to survey individuals and families with a cancer-predisposing genetic mutation in terms of their knowledge and opinions on fertility preservation and PGT-M, as well as identify key factors that impact decision-making.

Ongoing study

- If want to participate, please refer to postcard in tote with link to study.
Preliminary Findings

- Of those familiar with PGT-M (44%), few (17%) stated they would consider using it.
- Most respondents (69%) were unaware that eggs cannot undergo PGT-M.
- Only 16% had consulted with a fertility specialist for family planning.
- Despite this, 44% were aware of fertility preservation and would freeze eggs/embryos prior to undergoing a risk reducing surgery.
- Top concerns included financial burden (70%) and psychological distress (49%).

Conclusions:
- There is an opportunity to increase awareness about reproductive options, particularly by OB/GYNs and geneticists who could implement early referral to a fertility specialist for counseling.
- Potential barriers to patients’ accessing available options may be alleviated by promoting access to fertility treatments (including IVF/PGT-M) and by a multidisciplinary approach involving psychological support.
Informational Needs Exist for BRCA Carriers Regarding Issues Related to Reproduction

- Despite our understanding of the medical implications of a BRCA mutation, there is limited data on how knowledge of carrier status influences decisions about reproduction and parenthood.
- BRCA carriers may benefit from reproductive counseling after being informed of their carrier status and therefore improve knowledge and allow improved decision-making about reproductive options.
Is Infertility Treatment Safe for BRCA Carriers?

- Women in the general population undergoing fertility treatments do not have increased future risk of developing breast or invasive ovarian cancer.
- Current literature to date suggests no increased risk of breast cancer or ovarian cancer in BRCA carriers undergoing fertility treatments.

Treatment of infertility does not increase the risk of ovarian cancer among women with a BRCA1 or BRCA2 mutation


Long-Term Safety of Letrozole and Gonadotropin Stimulation for Fertility Preservation in Women With Breast Cancer

Jayeon Kim, Volkan Turan, and Kutluk Oktay

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Conclusion: COSTLES is unlikely to cause a substantially increased recurrence risk in breast cancer during the 5 years after diagnosis. U Clin Endocrinol Metab 101: 1364–1371, 2016
Options For Women With a BRCA Mutation Who Plan on Utilizing PGT-M at Some Point in the Future and Families Are Not Yet Complete

Ovarian Reserve

- Diminished ovarian reserve
  - Single
    - Egg Freezing
  - Married
    - IVF/PGT-M/Embryo banking

- Normal ovarian reserve
  - Single
    - Egg freezing
    - If Age <35
      - Annual monitoring of ovarian reserve
  - Married
    - IVF/PGT-M/Embryo banking
    - If Age <35
      - Annual monitoring of ovarian reserve
Options For Women With a BRCA Mutation Who Do Not Plan on Utilizing PGT-M and Families Are Not Yet Complete

**Ovarian Reserve**

**Diminished ovarian reserve**
- **Single**
  - Egg Freezing
  - If Age <35
    - Annual monitoring of ovarian reserve
  - Try to conceive
- **Married**
  - IVF/Embryo banking
  - If Age <35
    - Annual monitoring of ovarian reserve
  - Try to conceive

**Normal ovarian reserve**
- **Single**
  - Egg freezing
  - If Age <35
    - Annual monitoring of ovarian reserve
- **Married**
  - IVF/Embryo banking
  - If Age <35
    - Annual monitoring of ovarian reserve
  - Try to conceive
Scenarios

• I am a 30 year old BRCA carrier who is single and in the future I would like to prevent passing on this mutation, what can I do now?
  - She can freeze her eggs now. In the future she can thaw her eggs, fertilize them, and then undergo PGT-M.

• I am a 33 year old BRCA carrier who is married. We would like to have 2 kids in the future, but we’re not ready right now- maybe in 2 more years. We would also like to prevent passing on this mutation, what can we do?
  - The couple can freeze embryos now after undergoing. When the couple is ready to start their family, they can undergo a frozen embryo transfer of a single embryo that is unaffected and chromosomally normal.
Scenarios

• I am a 39 year old, recently diagnosed BRCA carrier who is single and plan on undergoing a risk-reducing BSO in the near future. I would like to have kids in the future. What are my options?
  - She can freeze her eggs now prior to a risk-reducing BSO.

• I am a 37 year old, recently diagnosed BRCA carrier who just got married. I would like to undergo a risk-reducing BSO soon but ideally would like to have 2 kids. What are my options?
  - The couple can freeze embryos now prior to a risk-reducing BSO an also have the option of undergoing PGT-M if interested. When the couple is ready to start their family, they can undergo a frozen embryo transfer cycle.
Caring for BRCA Carriers: Strategies to Promote Health and Preserve Fertility

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Summary

• Despite our understanding of the medical implications of a BRCA mutation, there is limited data on how knowledge of carrier status influences decisions about reproduction and parenthood.

• Women at risk for development of cancer need health care professionals to discuss not only the medical implications of their carrier status or risk-reducing options, but also information regarding fertility preservation and PGT-M.

• BRCA carriers may benefit from reproductive counseling after being informed of their carrier status and therefore improve their knowledge and allow improved decision-making about reproductive options.

• No ‘one-size-fits-all’ treatment option exists.