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Staff

Sue Friedman, DVM
Executive Director

Lisa Rezende, PhD
VP, Education

Diana Rose
Director, Volunteer Programs

Lisa Schlager
VP, Community Affairs

Kathy Steligo
Editor

Contributors

Marleah Dean Kruzel, PhD

Susan Lilly

Melanie Nix

Contact Us

FORCE
16057 Tampa Palms
Blvd. W. #373
Tampa, FL 33647

Tel: 866-288-RISK
Fax: 954-827-2200
info@facingourrisk.org
www.facingourrisk.org

Our Goal to Enroll: Helping to Accelerate Research

by Sue Friedman

People affected by hereditary breast and ovarian cancer (HBOC) frequently ask us, "What can I do to help accelerate research?" Research is critically important to improve medical care. HBOC research is challenged by the fact that our community is a subset of the larger cancer community; finding enough volunteers to complete HBOC research studies is critical. Our new "Goal to Enroll Campaign" encourages every adult affected by hereditary cancer to participate in HBOC-specific research.

To help reach our research goals, FORCE is building the "ABOUT Network," the first national research registry created *by* and *for* the HBOC community. ABOUT is part of a gigantic national resource that will include 70 million patients; this enormous pool of participants will allow us to conduct large research studies that have never before been possible. Input from members of our community will guide ABOUT research to answer questions that people affected by HBOC face every day. You are eligible to join if you are

an adult from an HBOC family, whether you are a survivor or previvor, whether or not you have had genetic testing, and if tested, whether your results were positive or negative for BRCA, PTEN, PALB2 or another mutation linked to cancer.

Enrollees complete a questionnaire about their health, medical decisions, and quality of life. This information will help us answer HBOC research questions and help to improve health outcomes; it will also allow us to notify each participant of studies that might be of interest based on their personal profile. Enrolling is easy: *the entire questionnaire takes only about 20 minutes.*



Visit aboutnetwork.org for enrollment information.

Joining FORCEs Conference Highlights

by Sue Friedman

Our 2014 conference was a record-breaking success! We welcomed 730 survivors, previvors, supporters, researchers, and health care providers to the largest annual gathering of the HBOC community. This issue features recaps of several sessions.

We're already preparing for next year: June 18-20, 2015 in Philadelphia, PA—check out our new conference logo below! Once again we will bring you world experts who will present the latest on all aspects of HBOC. Network with others

who live with HBOC, meet one-on-one with researchers and clinicians, and enjoy after-hours events, including our popular Show & Tell room. We will offer more than 40 sessions, including longstanding favorites: nonsurgical options for cancer detection and prevention, understanding mastectomy and reconstruction, new treatments for hereditary cancers, risk management for men with mutations, fertility issues, how to participate in and influence research, sexuality, managing menopause with and without hormones, long-term survivorship, and many more. Two new sessions will focus on timely topics: newly identified gene mutations and panel testing for cancer risk, and a forum on population-based BRCA testing.

Registration will open before the end of 2014 at facingourrisk.org/conference.



A New Resource: Talking about BRCA in Your Family Tree

by Susan Lilly

FORCE and the National Society of Genetic Counselors Cancer Special Interest Group recently published a new booklet entitled *Talking About BRCA in Your Family Tree*. The free booklet helps parents discuss BRCA-related issues with their children and loved ones. The booklet includes quiz-like assessments that guide self-discovery through knowledge sharing.

Talking About BRCA in Your Family Tree:

- helps parents gather the facts they need to be comfortable discussing these issues in family settings.
- provides guidance for communicating with children based on their age and developmental stage.
- gives helpful tips about discussing BRCA with children.

One recommendation suggests that it's best to think about the communication process as gradual rather than a one-time event. The important thing to remember is that every child, parent, and family situation is unique. Using the booklet as a guide, parents can craft their conversations to suit their family's needs.

Talking About BRCA in Your Family Tree points readers to several online and print resources to help families learn more about BRCA mutations and hereditary cancers. To access the booklet, please visit: facingourrisk.org/children.



Conference Recap: Sharing Genetic Information with Children

by Susan Lilly

Dr. Angela Bradbury (Basser Research Center, University of Pennsylvania) presented information along with two other panelists, Lisa Schwartz, Ph.D. (Children's Hospital of Philadelphia), and Linda Patrick-Miller, Ph.D. (Center for Clinical Cancer Genetics and Global Health, University of Chicago) about the results of sharing BRCA mutation status with children.

Current guidelines state that children under the age of 18 should not be tested for BRCA mutations because the increased cancer risk applies to adults. However, Dr. Bradbury acknowledged that elegant arguments exist on either side of the debate. Screening guidelines for women with mutations begins at age 25, except in cases where the family history includes breast cancer in the early 20s.

Dr. Bradbury discussed results of the Evaluating Parent to Offspring Communication for Hereditary Disease (EPOCH) study. The good news is that the majority of children were not distressed by their parent's positive test results. Not surprisingly, a small but significant percentage of children felt concern (13%) or stress (11%) if results were positive or a "variant of uncertain significance."

The Study of Female Teens (SOFT) is a survey study for mothers and their 11- to 19-year-old daughters to learn what girls know about breast cancer risk, and how their thoughts and feelings change over time. Adolescence is a time of rapid growth, and development and teens can be vulnerable to toxins and exposures that could increase their risk for cancer later in life. Generally girls are aware of things they can do to reduce their breast cancer risk. So far, SOFT results show that mothers are the primary information source for their daughters, and the more anxious and worried mothers are, the more likely their daughters will feel the same. Outreach efforts should focus on helping these mothers communicate their status to their daughters.

Dr. Schwartz cautioned parents to think about their adolescent children as individuals with unique needs before deciding what to reveal and when. Because the teenage brain is a work in progress, parents should consider the behaviors that might result from divulging the

distressing news. Some teens will not feel stressed at all, while others will have significant worry. The goal for the parent is to "neutralize" negative beliefs. Parents can play a powerful role in shaping their offspring's reactions.

Finally, Dr. Patrick-Miller gave some practical advice to all the parents and grandparents in the session: "Put your oxygen mask on first." In other words, taking care of yourself provides you with the best opportunity to take care of

"...the majority of children were not distressed by their parent's positive test results."

and empower your daughters with strategies for healthy adaptation and managing lifestyle and risk reduction. Meeting with a genetic counselor can help you with this. Other tips include:

- Let your child's age and maturity guide you.
- Communicate directly with your child; the worst way to hear something is to overhear it.
- Use correct terminology; euphemisms can be confusing.
- Sharing your feelings is OK. It gives your child permission to do the same.
- Respect your child's preference to talk or not to talk.
- Welcome your child's questions.
- Answer sincerely. "I don't know, but we can find out" might be the most appropriate answer.

Susan Lilly, MHS, has a professional background as a health researcher and writer. She joined the FORCE community upon discovering her BRCA2 mutation status after a breast cancer diagnosis in her early 40s.

Conference Recap: Hereditary Metastatic Breast Cancer Update

by Susan Lilly

Dr. Melinda Telli (Stanford University Medical School) presented on the latest clinical research for hereditary metastatic breast cancer (MBC). Treatment options are available, with the goal of improving survival, alleviating symptoms, preventing complications, and limiting toxicity while optimizing quality of life. Many women are long-term survivors of metastatic breast cancer.

Dr. Telli presented promising treatments that are currently being investigated in clinical trials. Cancer research is moving towards more individualized therapies, targeting tumor proteins and molecules called “biomarkers” to develop treatments that block cancer growth. BRCA mutations may become an important biomarker for treatment, but at present, outside of surgical decisions such as lumpectomy or mastectomy, mutation status is not used to guide breast cancer treatment.

Prior research suggests that BRCA-related cancers generally respond well to chemotherapy, however, little is known about which chemotherapy regimens offer the best outcomes for mutation carriers. We do know from small studies that PARP inhibitors, which block DNA repair in cancer cells, show promise

inhibitors are more effective than standard therapies. Open studies include BROCADE (veliparib), EMBRACA (BMN 673), BRAVO (neraparib) and OLYMPIAD (olaparib), which are currently recruiting patients to evaluate the effectiveness of PARP inhibitors with or without chemotherapy, and the ABRAZO study (BMN 673) that is open to those who have undergone many prior therapies for metastatic disease or who have previously received platinum. A trial of BMN 673 will also be launched in patients who do not have BRCA1 or BRCA2 mutations, but who do have other less common mutations associated with hereditary breast cancer, including PALB2, ATM, BARD1, BRIP1, and RAD51, among others.

A Spanish company, PharmaMar, is recruiting patients for trials of its new drug PMO1183 to treat BRCA1 and BRCA2 mutation carriers with MBC. PMO1183 is a DNA-damaging chemotherapy agent that attacks the cancer differently than platinum. It looks promising for BRCA-related cancers, and it does not cause hair loss.

Dr. Telli concluded by introducing immunotherapy, an area of research that she considers promising. It stimulates a person's own immune system to help fight and kill cancer cells. In the future, immunotherapeutic approaches might be particularly relevant in mutation carriers, but right now the research is ongoing.

FORCE has built a clinical trial search tool that is enriched with prevention, detection, treatment, and quality-of-life studies recruiting people with HBOC. The tool allows you to search by type of study, city or region, type and stage of cancer, and type of research. Visit facingourrisk.org/enroll to search for studies.

You can find a list of featured research studies open to people with metastatic hereditary breast cancer on the FORCE website at facingourrisk.org/featured.

“PARP inhibitor clinical trials for patients with advanced breast cancer are ongoing.”

for BRCA1 and BRCA2 mutation carriers with advanced breast cancer, but they have not yet been approved by the FDA. In addition, small studies show that platinum chemotherapy (e.g., cisplatin) is very active in BRCA-related breast cancers. Based on these findings, the question of whether BRCA status should be used as a biomarker for treatment selection is being studied by oncologists.

PARP inhibitor clinical trials for patients with advanced breast cancer are ongoing. Many large studies that are underway could lead to FDA approval if they show that PARP

FORCE Participates in the Metastatic Breast Cancer Alliance

by Diane Rose

A new patient movement is focused on drawing attention to metastatic breast cancer, a subject that has been in the news recently. At the forefront of this effort is the Metastatic Breast Cancer Alliance, a consortium of organizations who have joined together to assess and address the unmet needs of this community.

The Metastatic Breast Cancer (MBC) Alliance (mballiance.org) was formed in 2013, when FORCE and other advocacy organizations joined together to transform and improve the lives of women and men who live with metastatic breast cancer.

FORCE joined the efforts of the MBC Alliance to provide information on behalf of our community, and to share the combined knowledge of the Alliance with our constituents. The HBOC community supports many metastatic patients, as BRCA mutation carriers are more likely to develop breast cancer. This highlights the importance of FORCE efforts to recruit as many people as possible into HBOC-specific research to help find more effective treatments and to save lives.

MBC Alliance member groups recognized that despite the accomplishments of their respective organizations, they needed to unify and work together to assure that:

- all MBC patients and their caregivers know how to and can access the care and services they need from a responsive and well-informed healthcare system.
- those diagnosed, their families, health care providers, researchers, health policy influencers, and policy makers understand MBC and how it differs from early-stage breast cancer.
- progress with research focuses on extending life, enhancing quality of life, and ultimately ending death from the disease.

Diane Rose is the Director of Volunteer Programs for FORCE, providing training and resources for our 53 support groups across the United States and Essex, UK.

Looking for Answers to Your HBOC Questions? Participate in Our Surveys

by Lisa Rezende, PhD

Individuals facing hereditary breast and ovarian cancer (HBOC) work with their doctors to make decisions on managing risk and treating disease. Some of the decisions can be based on decades of research and carefully crafted clinical guidelines. But in some cases, there is not enough research to guide decisions that people with HBOC face every day. FORCE and the ABOUT Network are conducting a series of anonymous surveys to find out how you make medical decisions about HBOC treatment, prevention, detection and quality of life.

Our first survey looked at how women decide whether or not to remove their uterus at the time of risk-reducing surgery to remove ovaries and fallopian tubes. No national guidelines recommend for or against hysterectomy for women with BRCA mutations, yet women frequently turn to FORCE for information and support to help them sort through this dilemma and make the decision that is right for them.

The survey has provided us with insights into how high-risk women make decisions about hysterectomy. We learned that:

- about half of women had their uterus removed at the time of risk-reducing surgery.
- a doctor's recommendation is the most frequent factor that influences women's decision to remove or not to remove their uterus.
- concerns about uterine cancer risk and prior uterine abnormalities such as fibroids influenced women's decisions to remove their uterus.
- concerns about possible side effects and surgical complications influenced women's decisions to keep their uterus.
- many women who are considering surgery expressed uncertainty about whether or not to remove their uterus.

This survey (<https://www.surveymonkey.com/s/GRDJTQ7>) and a follow-up survey on decision making regarding hormone replacement therapy (<https://www.surveymonkey.com/s/CYDGM7V>) are currently open. The results of these surveys will help us to develop research studies to learn which medical decisions provide the best outcomes, and to develop education programs to address gaps in knowledge.

Voices o

In each issue, we'll invite a FORCE member with a valuable experience, or a touch of insight, dealing with issues of hereditary cancer.

Get Off the Sidelines and Help Win the War on HBOC

by Melanie Nix



Melanie Nix

I'm participating in the ABOUT Network because it benefits the HBOC community. My mother always encouraged me to get off of the sidelines. Twenty-four years after her death from metastatic breast cancer when HBOC information was in its infancy, I'm still guided by her words.

A few months before my triple-negative breast cancer diagnosis, I learned that I had a BRCA1 gene mutation. My mind swirled with questions, especially about the impact on my young children, who both have a 50% chance of carrying the same mutation. Seeking

opportunities to affect change, I applied for membership on the Advisory Panel on Patient Engagement for the Patient-Centered Outcomes Research Institute (PCORI). My appointment allows me to help ensure patient engagement in research. I've also applied for the ABOUT Network's Steering Committee, so that I can actively play a role in the registry's success.

The ABOUT Network participates in the PCORI national research network known as PCORnet, and represents significant opportunities for progress:

- Its association with PCORI ensures patient-guided research.
- It is inclusive, targeting diverse groups that will provide rich data.
- Patients are essential stakeholders with a critical role throughout the research process.
- The research can drive greater focus on HBOC.

My children can benefit from research that is being fueled through the ABOUT Network. So can I. It can help them make choices that my mother never had. We will only win the war on cancer if we stay off the sidelines.

Melanie A. Nix, mutated BRCA1 gene carrier and triple-negative breast cancer survivor by age 38, is cofounder of the Breast Cancer Comfort Site (breastcancercomfortsite.com), a virtual wellspring from which breast cancer patients and survivors can gain nourishment and guidance through their metamorphosis from patient to victor.

f FORCE

Member to share an insightful perspective, your story to help others who are affected by hereditary breast and ovarian cancer

A Powerful FORCE for Research

by Marleah Dean Kruzal, PhD



Dr. Marleah Dean Kruzal

When I was eight, my mother found a barely noticeable breast lump. I watched her undergo surgery, chemotherapy, nausea, hair loss, radiation, and reconstruction. Though scared, I was determined to be involved in her recovery, as much as an eight-year-old could be.

Becoming involved has helped me cope with my own high risk of cancer. That eight-year old girl became a professor in Health Communication at the University of South Florida. My research explores BRCA+ patients' experiences in decision making and managing an uncertain future. I also volunteer for the FORCE helpline. Most recently, I enrolled as a participant in the ABOUT Patient-Powered Research Network.

Traditionally, researchers pose questions and hypotheses. ABOUT seeks patients who are affected by HBOC, asking them about their health decisions, outcomes, and unanswered medical questions, and then conducts research to answer those questions and concerns (see sidebar). This information will be used to improve research on patient health decisions, subsequently assisting women in making such decisions.

“Every person has something to offer ABOUT and the HBOC community.”

As a researcher, I understand that research is the path to improve medical care. As a BRCA2 previvor, I enrolled in the ABOUT registry as a powerful way to give back to my community. As a professor of Health Communication, I have applied for the ABOUT Steering Committee to use my expertise to inspire others to join the network and assure it's success. I am not unique. Every person has something to offer ABOUT and the HBOC community. As patients, we are the experts who hold the key to improving our health outcomes. If you would like to be involved in ABOUT, visit facingourrisk.org/registry.

Dr. Marleah Dean Kruzal is an Assistant Professor in Health Communication at the University of South Florida in Tampa, FL.

Share Your Story

Do you have something to say that may inform our readers or ease their experience? We invite you to share your reflections or personal story about dealing with the issues of hereditary breast or ovarian cancer. Tell us how you feel, how you cope, or what you've learned. E-mail stories of 500-550 words to info@facingourrisk.org or mail to FORCE, 16057 Tampa Palms Blvd. W., Tampa, FL 33647. Please include your name and daytime telephone number so we can contact you if we decide to publish your story in a future issue.

FORCE Research Advocate Training and Consumer Engagement in HBOC Research

by Lisa Schlager

In the past, the only role for patients and non-scientists in the research process was to volunteer as a subject in research studies. This is changing. There is increasing recognition of the value of input from the general population and patient communities being researched to weigh in on the development and direction of research studies. The ABOUT Network provides unprecedented opportunities for members of our community to help influence the research process.

FORCE's Research Advocate Training (FRAT) Program is a basic educational course that helps prepare people with no formal science training to participate in research advocacy on behalf of the HBOC community. The program consists of a series of expert-led webinars and live meetings on topics including basic cancer, breast and ovarian cancer, genetics, statistics, clinical trials and research, patient protection, ethics, and government regulatory processes. Participants complete the program at their own pace. FRAT graduates are notified about advocacy opportunities for which they may qualify.

Opportunities to be engaged in the governance of the ABOUT Network are open to FRAT graduates, including participation in our Steering Committee and/or three work groups:

- Research Generation and Prioritization
- Promotion and Recruitment
- Engagement and Retention

For more information about the FRAT program, visit the Research Advocate Program page on our website or contact Lisa Schlager at: LisaS@facingourrisk.org.

Lisa Schlager is Vice President of Community Affairs at FORCE. A BRCA1 previvor, she lives in the DC area with her husband and two children.

Conference On-demand Videos Available Online

by Lisa Rezende, PhD

Several important talks from the 2014 Joining FORCES conference, including the session highlighted below, are available online (facingourrisk.org/conference).

Long-term Consequences of Menopause

Risk-reducing salpingo-oophorectomy (RRSO) has been shown to decrease the rate of ovarian cancer and increase lifespan in women with BRCA mutations, but the surgery shifts premenopausal women into immediate menopause. Dr. Susan Domchek (Basser Center for BRCA) and Dr. Neill Epperson (Director, Penn Center for Women's Behavioral Wellness) presented the latest research on the long-term effects of menopause.

Dr. Domchek's study of the long-term consequences of surgical menopause after RRSO found that more than 50% of patients had issues with bone loss, stress, hot flashes, decreased libido, attention problems, and sleep loss.

Dr. Epperson discussed the "post-RRSO brain," detailing the cognitive effects of early menopause on women who undergo RRSO. She noted that:

- loss of estrogen at a young age affects cognitive function.
- some women are at risk of depression after menopause.
- women with early-life adversity are at increased risk of mood and cognitive problems.

Other available video-on-demand titles include:

- Patient-Powered Research Networks
- Menopause With and Without Hormones
- Pancreatic Cancer Detection, Prevention, and Treatment
- Update on Targeted Therapies
- Complementary and Integrative Medicine for Symptom Management
- Putting It All Together to Make Decisions
- What's New in HBOC Research?

Reference

Arts-de Jong M, Mass AH, Massuger LF, et al. "BRCA1/2 mutation carriers are potentially at higher cardiovascular risk." *Critical Reviews in Oncology/Hematology*, published online February 18, 2014.

Heart Disease in BRCA Mutation Carriers

by Lisa Rezende, PhD

While managing cancer risk is a priority, BRCA mutation carriers are often concerned about their risk of heart disease—the leading cause of death for American women—and how their mutation or risk-management choices may impact their cardiovascular health.

Although much of the risk for cardiovascular disease comes from lifestyle and genetic factors unrelated to BRCA mutations, some breast cancer treatments (including certain chemotherapies and medications like Herceptin) also raise risk. It is unclear whether early menopause contributes to an increased chance of heart disease. Some early research also suggests that BRCA genes may be important in repairing damage to heart cells, leading to speculation that women with mutations, even those who do not receive chemotherapy or undergo early surgical menopause, may have elevated likelihood for heart disease. A recent paper reviewing these risks called for more research into the chance of heart disease in BRCA mutation carriers.

Risk of heart disease associated with surgical menopause

Risk-reducing salpingo-oophorectomy (RRSO) increases survival of BRCA mutation carriers. Experts recommend RRSO for women with BRCA mutations: around age 35 for BRCA1 mutation carriers and around age 40 for BRCA2 mutation carriers, after completion of childbearing. How does this affect their risk of heart disease? Several studies suggest but have not proven that a woman's risk of heart disease increases after menopause. Complicating matters further, surgical menopause may affect body mass index (BMI), blood lipid profiles and other risk factors for cardiovascular disease. Women in surgical menopause should consult with their health care professional about how they can manage their risk of heart disease.

Research demonstrates that women with BRCA mutations who remove their ovaries survive longer than women with mutations who do not. So, despite concerns about a potentially increased risk of heart disease associated with early menopause, women with BRCA mutations are strongly advised to remove their ovaries.

Risk of heart disease associated with chemotherapy

Some experts question whether BRCA mutation carriers may be more sensitive to numerous breast cancer chemotherapy drugs that are known to increase the short-term and long-term risks of cardiovascular disease in the general population. Further research is needed to learn whether BRCA mutation carriers who receive chemotherapy are at higher lifetime risk of heart disease, and to identify the best chemotherapy regimen for mutation carriers diagnosed with cancer.

Are all BRCA mutation carriers at increased risk of heart disease?

Whether or not BRCA mutations alone affect cardiovascular health is still unknown. BRCA and other HBOC-related genes help to repair DNA damage, keeping cells healthy and protecting them from cancer. Some experts believe that these genes may also protect organs such as the heart from damage. Studies of mice show that BRCA gene changes may be associated with higher

"Some early research suggests that BRCA genes may be important in repairing damage to heart cells..."

mortality after heart attacks. The results must be confirmed in humans before we know if BRCA mutation carriers are at an increased risk of heart disease.

Making healthy lifestyle choices reduces the risk of heart disease. Whether you have a BRCA mutation or not, it is wise to stop smoking, maintain a healthy body weight, engage in a regular exercise program, know your family history of heart disease, and speak with a health care provider about monitoring cardiovascular health.

Improving Ovarian Cancer Screening

by Lisa Rezende, PhD

Many women with mutations in BRCA1 or BRCA2 undergo close screening for ovarian cancer until they complete childbearing and/or reach age 35-40, when surgical removal of ovaries and fallopian tubes (risk-reducing salpingo-oophorectomy) is recommended. Current National Comprehensive Cancer Network (NCCN) guidelines recommend that BRCA1 or BRCA2 mutation carriers with intact ovaries consider ovarian cancer screening twice a year using pelvic exam and transvaginal ultrasounds, and a blood test to look for increases in the CA-125 protein.

“The study shows the potential of using HE4 as a biomarker to confirm elevated CA-125 values.”

While these tests are the best we have, they are far from perfect. Even with heightened screening, ovarian and fallopian tube cancers are usually found at late stages (stages 3 or 4). This means that a woman can have normal images on transvaginal ultrasound and normal CA-125 levels but still have cancer. Some women have false positive results: abnormal findings on transvaginal ultrasounds and elevated CA-125 levels even when no ovarian cancer is present, resulting in more extensive testing, and in some cases, surgery to confirm that the changes are cancerous.

Finding better methods to detect ovarian cancers before they progress is a high research priority for our community. Ideally, a good biomarker for screening would:

- show changes at the early stages of ovarian cancer.
- be measurable in the bloodstream (blood tests are relatively noninvasive and inexpensive).

Scientists are searching for new biomarkers that may indicate early-stage ovarian cancer. One candidate is a protein known as HE4. Early studies looked at women with both benign and cancerous pelvic masses, and compared their CA-125 to HE4 blood test results. HE4 levels identified more ovarian cancers than CA-125 alone. While this study pointed to the promise of HE4 as an ovarian

cancer biomarker, proving that it is useful as an ovarian cancer screening test in patients without symptoms requires further research.

Another study tested the use of HE4 combined with CA-125, either as an initial screening test or using HE4 levels to confirm abnormal findings on CA-125. The study included 1,172 women at high risk for ovarian cancer from one or more of the following:

- a BRCA1 or BRCA2 mutation
- a strong family history of ovarian cancer
- other ovarian cancer risk factors

The women were randomly assigned to one of two groups. The first group initially had blood tests to determine levels of both HE4 and CA-125. The second group was initially screened using CA-125 alone; HE4 levels were then tested only if the CA-125 values were abnormal. Both groups were given transvaginal ultrasounds if they had elevated CA-125 and/or HE4 levels.

Over three years, 37 of the women had at least one abnormal screening (transvaginal ultrasound, CA-125, and/or HE4). Six of the women identified through screening had surgery to remove their ovaries and fallopian tubes, and two were diagnosed with ovarian cancer at the time of surgery. Among women with abnormal findings during screening:

- both women who had abnormal findings on all three screens (transvaginal ultrasound, and elevated CA-125 and HE4 levels) were diagnosed with ovarian cancer at the time of surgery.
- both ovarian cancers uncovered during screening were advanced (stage 2c or 3c).
- two women with elevated CA-125 values but normal HE4 values and normal transvaginal ultrasound images were later diagnosed with other cancers (one recurrent breast cancer and one pancreatic cancer).
- one woman with elevated CA-125 and HE4 values but normal transvaginal ultrasound images was later diagnosed with lung cancer.

Over the course of the study, 102 women with normal screening results elected to have their ovaries and fallopian tubes removed to reduce their cancer risk. Of these women:

continued on page 8

References

Moore RG, Brown AK, Bast RC, et al. “The use of multiple novel tumor biomarkers for the detection of ovarian carcinoma in patients with a pelvic mass.” *Gynecological Oncology* vol. 108, no. 2 (2008): 402-8.

Karlan BY, Thorpe J, Urban N, et al. “Use of CA-125 and HE4 serum markers to predict ovarian cancer in elevated-risk women.” *Cancer Epidemiology, Biomarkers, and Prevention* vol. 23, no. 7 (2014): 1383-93.

Conference Recap: “What’s New in HBOC Research?”

by Lisa Rezende, PhD

Dr. Mark Greene (Clinical Genetics Branch of the National Cancer Institute) presented research from the National Ovarian Cancer Prevention and Early Detection Study (GOG-0199).

The GOG-0199 study asked high-risk women (those with BRCA1/2 mutations or a very strong family history of breast and/or ovarian cancer) to make a choice: either remove their ovaries and fallopian tubes to reduce cancer risk, or undergo enhanced screening using an investigational strategy with CA-125 known as the ROCA model. ROCA follows CA-125 over time to determine whether rising levels can be used to detect ovarian cancer earlier than the standard use of CA-125, which simply classifies each test as normal or abnormal.

The study found that:

- premenopausal women had higher normal baseline CA-125 levels than postmenopausal women.
- the upper limit of normal CA-125 for premenopausal women who are not on oral contraceptives is approximately 50 units per milliliter (U/ml).
- normal CA-125 for postmenopausal women is up to 35 U/ml (the current standard).

Examining tissue from women who underwent risk-reducing salpingo-oophorectomy showed that:

- 4% of BRCA mutation carriers unexpectedly had cancer at the time of their surgery.
- postmenopausal women were more likely to have cancer.
- 14 of 21 cancers found were early stage (stages 0, 1, or 2).

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Your generous donations allow us to provide this newsletter at no charge to people at high-risk. Philanthropic support is critical to FORCE's survival and ensures our continuing ability to provide publications like our newsletter to our community. Your charitable gift can help save lives—please consider making your gift today! To learn more about helping FORCE, visit www.facingourrisk.org/how_to_help.

This Joining FORCE's newsletter was made possible by a generous grant from Genentech

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We Want to Hear From You

What's on your mind? What would most help you understand or cope with issues of prevention, diagnosis or treatment? Perhaps you've recently tested positive for a BRCA gene mutation and don't know where to turn. Maybe you're dealing with breast or ovarian cancer, or care about someone who is. Send your input, ideas and comments to info@facingourrisk.org or mail to FORCE, 16057 Tampa Palms Blvd. W., Tampa, FL 33647.

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Improving Ovarian Cancer Screening *continued*

- five were diagnosed with precancer (stage 0) or early-stage (stage 1a) ovarian or fallopian tube cancer or pre-cancer at the time of surgery.
- one woman who was diagnosed with fallopian tube cancer had elevated CA-125 levels before surgery.

The study shows the potential of using HE4 as a biomarker to confirm elevated CA-125 values. While this is an early study, the authors note that using HE4 as a primary

screening test increased false positive results. However, using it as a secondary test to follow up an abnormal CA-125 result showed more promise, and could decrease false positives generated by using CA-125 alone. This study was relatively small, few cancers were detected, and screening did not identify any early (stage 1) cancers. More research is needed before the use of additional biomarkers in ovarian cancer screening is recommended.

What's New @ FORCE

New FORCE Website

Have you visited FORCE lately? Our new website is now live at facingourrisk.org. We've simplified the navigation to help you more quickly find the information and resources you need. Review more than 1,000 pages of expert-reviewed educational materials, on-demand webinars, taped conference sessions, and the latest research.

FORCE Receives a CDC Grant for the XRAYS program

What does the latest research mean for our community? We will expand our coverage of new and emerging research through a grant from the CDC. Our Examining the Relevance of Articles for Young Survivors (XRAYS) program, made possible by the EARLY Act, will develop a system to rate the accuracy and relevance of media reports on new research.

