Welcome From Our Director of Education  
by Lisa Rezende, PhD

As the new Director of Education at FORCE, I am thrilled to have the opportunity to combine my personal experience as a BRCA1 mutation carrier and my professional experience in biomedical research and science education to work for the benefit of the hereditary breast and ovarian cancer (HBOC) community. I am passionate about helping our community navigate through the amazing array of FORCE educational materials, developing new resources to meet the growing needs of families facing hereditary breast and ovarian cancer, and translating the latest research into information that people can use to make medical decisions and improve their health.

In this issue, we cover the different types of negative BRCA test results and review improvements in genetic testing that may help people to better understand their risk for cancer. You'll also learn about our collaboration with University of South Florida researchers to create a “patient-powered research network” known as ABOUT. We will turn to members of our community to help us identify and prioritize the critical questions that people facing hereditary cancer need answered to make detection, prevention, treatment and quality-of-life health care decisions.

Read on page 2 about our first spring Live Life Empowered fundraiser and a preview of our 8th annual Joining FORCEs Conference.

If you have questions about hereditary cancer risk management, treatment, or research, I want to hear from you. Please contact me (lisar@facingourrisk.org) with topics you would like FORCE to address on our website or in future newsletters. I look forward to learning what's important to you to better serve our constituency.

ABOUT Patient-Powered Research Network  
by Sue Friedman

FORCE has collaborated with researchers at the University of South Florida and the Michigan Department of Community Health to form the ABOUT Patient-Powered Research Network (PPRN). Our intent is to improve informed decision making and health outcomes for people affected by hereditary breast, ovarian and related cancers. Unlike traditional research that involves patients only as research participants, ABOUT will conduct "patient-centered" outcomes research involving consumer participation in every aspect. We plan to enroll 10,000 people, build a network governance structure that includes patients and advocates, and compile and refine people's real-world experiences to shape and prioritize the important research questions.

Research driven by patients and their real-world experience is not new, but the Patient-Centered Outcomes Research Institute (PCORI), the government-funded agency focusing on it, is new. The priority is conducting research to answer four common patient questions:

• Given my personal characteristics, conditions, and preferences, what should I expect will happen to me?
• What are my options, and related potential benefits and harms?
• What can I do to improve outcomes that are most important to me?
• How can my health care providers help me make the best decisions about my health and healthcare?

The ABOUT Network was one of 18 PPRNs funded by PCORI (and the only PPRN focused on hereditary cancer) to participate in PCORnet, PCORI's national research network that will conduct large-scale patient-centered outcomes research.
FORCE 8th Annual Conference Sponsors

We are very grateful for the generous sponsors who make our 8th Joining FORCEs conference possible:

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It’s Conference Time Again!
by Sue Friedman

It seems like yesterday when we closed our 2012 conference in Orlando with the announcement that our next conference would be Spring 2014 in Philadelphia. And now here we are 19 months later preparing for our 8th annual Joining FORCEs conference. Attendance for the event has already surpassed the 600 men and women who took part in 2012, making this the largest gathering of the BRCA and HBOC community.

Conference highlights and updates include:
• Screening two exceptional films of importance to our community: In the Family, with filmmaker Joanna Rudnick on hand to answer questions, and Decoding Annie Parker—we are honored to have Annie Parker herself join us for a post-film discussion.
• Filming of some of our speakers and sessions by producer Alan Blassberg for the documentary Pink and Blue.
• Updates of how FORCE is leading the patient-powered research movement for the HBOC community through our ABOUT Network collaboration.
• Recording some sessions for on-demand viewing for those who cannot attend.
• Summaries of the latest research and standard of care for prevention, detection, treatment, and improved care for people facing hereditary cancers.
• An opportunity for conference attendees to participate in HBOC-specific research, and to meet one-on-one with world experts.

Watch for our fall newsletter for recaps of the conference and summaries of specific sessions.

FORCE Debuts a Springtime NYC Celebration: Live Life Empowered
by Tina Krall

Kara DioGuardi, GRAMMY-nominated songwriter, Warner Bros. executive, Arthouse Entertainment music publisher, and former American Idol judge; and Stacey Sager, Channel 7 Eyewitness News reporter and two-time cancer survivor, co-hosted FORCE’s inaugural Live Life Empowered spring celebration at Hudson Terrace on April 30. Funds raised from the event will support the needs of women, men and families affected by hereditary cancer.

The fundraiser marked FORCE’s first major event in New York City. DioGuardi, who is a previvor, shared her personal story; she credits Sager for educating her and possibly saving her life. After watching a news segment that included Ms. Sager’s discussion of her own BRCA status, preventative oophorectomy, and discovery of early-stage fallopian tube cancer, Ms. DioGuardi pursued genetic testing and learned that she carries a BRCA 2 mutation.

Live Life Empowered attendees braved stormy weather to share an evening of fantastic food, and enjoyed DioGuardi’s special performance of some of her well-known hits including songs written for Pink, Kelly Clarkson, Ashlee Simpson, and other recording artists. DioGuardi delivered a perfect performance and introduced each song with anecdotes about each songwriting session.

Tina Krall is FORCE’s Senior Vice President of Development and oversees all fundraising efforts to support FORCE’s work with the HBOC community.
New Tools Help Patients with Uncertain or Negative BRCA Results
by Lisa Rezende, PhD and Sue Friedman

BRCA test results sometimes don't provide clear answers about cancer risk. Several types of BRCA tests can produce varying results, which have different health implications. This is why genetic counseling before and after genetic testing is so important.

True Negative
When a family member tests positive for a BRCA mutation, that particular mutation is known to be the cause of cancer in that family, and other blood relatives can then be tested for the same mutation. Anyone who tests negative for a known mutation in their family is considered a "true negative." Their risk for cancer is similar to the risk for cancer in an average person (see our related article “Weighing the Evidence” in this issue).

Uninformative Negative
Mutations in BRCA1 and BRCA2 account for about half of all hereditary breast and ovarian cancers; many families who may experience a lot of cancer have no known mutation. In families who have multiple diagnoses of breast and/or ovarian cancer, when all members test negative for a BRCA mutation, their results are categorized as “uninformative negative” because the negative test does not indicate anything about family members’ cancer risk.

In addition to BRCA1 and BRCA2, mutations in other genes can cause hereditary breast and ovarian cancers. Some, such as the genes that cause Lynch Syndrome, are part of known hereditary cancer syndromes. Others may be caused by mutations in one or more genes that somewhat increase cancer risk, and result in higher risk when inherited together.

Variants of Uncertain Significance
Some BRCA test results indicate a “variant of uncertain significance” (VUS). It is normal to have variations in genes, and some changes do not affect how the gene functions. Gene changes that cause a particular eye color, for example, do not affect vision. Similarly some changes in the BRCA genes can cause the gene to stop working, while other changes may be harmless variations that don't affect cancer risk. New tools and databases are being developed to help families with a BRCA VUS to better understand their risk of cancer (See the sidebar on page 7.)

Improvements in BRCA Testing
Since the availability of BRCA testing, the genetic testing technology has improved, and will likely continue to become more precise in the future. In the past, some tests failed to identify certain BRCA1 and BRCA2 mutations known as “rearrangements” as well as other mutations. Some families that previously tested as “uninformative negative” for BRCA in the past may benefit from expanded panels that look for newly identified BRCA mutations.

“...more research is needed to understand how a mutation in one of these genes, or a combination of mutations in several of these genes might affect cancer risk.”

Testing Multiple Genes to Assess Risk
If your family has a strong history of breast or ovarian cancer but has no known BRCA mutation, you have other testing options. A genetics expert can help you determine whether additional tests for specific genes, or new "multiplex panel testing" that scans several genes may provide additional information after a negative BRCA test.

Mutations in other genes can cause inherited breast and ovarian cancers, including PTEN (Cowden Syndrome), STK11 (Peutz-Jeghers Syndrome), TP53 (Li-Fraumeni Syndrome), CDH1 (hereditary diffuse gastric cancer), and a host of genes known to cause Lynch Syndrome.

Some new panel tests include mutations in dozens of genes that are not associated with a specific cancer syndrome but still may put an individual at a higher risk of cancer than the average person. Such panels look for mutations in genes such as PALB2, CHEK2, and ATM that are known to increase cancer risk. Not enough research has been conducted for some genes in these panels to identify that risk, and we have even less research on the best ways to manage risk for cancer in people who have mutations. Results from these tests are complicated, and more research is needed to understand how a mutation in one of these genes, or a combination of mutations in several

continued on page 7
About 18% of ovarian cancers are caused by a BRCA mutation. A recent search on clinicaltrials.gov—the government-maintained database for research enrolling patients—showed that out of 60 advanced ovarian cancer treatment studies in the United States, only 8 specifically targeted patients with BRCA mutations.

I'm getting great care at MD Anderson, and joining a Johns Hopkins vaccine clinical trial has improved my odds and made me a valuable research subject. Going forward, I now have two outstanding institutions that are familiar with my case to advise me.

David Dessert participates daily in pancreatic cancer message boards, providing a perspective as one of the few long-term survivors. He is taking Johns Hopkins data science and bio-statistics online courses to better understand clinical trial and study design and results.

I have participated in many other studies, authorizing my data and tissue samples to be used for research. If anything about my situation can be used to ensure that others in the future might be spared these diseases, I have to help.

Carey Fitzmaurice was diagnosed with Stage IIIC ovarian cancer in 2006 and Stage 2b breast cancer in 2008. She is the founder and president of Teal Toes, an organization created to raise awareness of ovarian cancer.

Understanding how to find studies and volunteer for research participation is equally challenging. You may hear about a trial going at the medical center where you receive your care, but is that study the best fit for you? Will it resolve questions that you and your family want answered about hereditary cancer?

FORCE is committed to making research enrollment as easy as possible for our community. We have developed a research and clinical trial search tool (facingsign.org/researchtool) that helps to match people facing hereditary cancer with research studies that are specifically designed to understand hereditary cancer. The database includes studies on breast, ovarian, fallopian tube, prostate, melanoma, and pancreatic cancers. Studies can be searched by region, cancer site, phase of research, and trial type (prevention, detection, treatment, and quality of life). We will be updating the tool regularly, so please keep checking for new studies in your area.

More general advanced ovarian cancer clinical trials draw from women with and without BRCA mutations.
Patient-Centered and Real World Research

Much of the research to date has been conducted at large academic institutions and cancer centers. Not all patients have access to these centers. Less is known about patient care and outcomes at smaller facilities, in rural settings, and in private practices, despite the fact that most people receive care in these settings.

People who wish to participate in research are often excluded if they do not have access to large academic institutions. Patient-Centered Outcomes Research Institute (PCORI) prioritizes data collection of patients who receive care in these real world settings. Our ABOUT Patient-Powered Research Network allows anyone who is affected by hereditary cancer to participate in the research process regardless of where they live and where they received their care (read our article on ABOUT on page 1).

References


Weighing the Evidence: Are Women Who Test True Negative for BRCA at Increased Risk of Cancer?

by Lisa Rezende, PhD

BRCA tests can produce a few types of negative results (see “New Tools Help Patients with Uncertain or Negative BRCA Results” on page 3). When relatives test negative for a known BRCA mutation in their family, the result is known as a “true negative.” Women with a true negative result are usually advised that their breast and ovarian cancer risk is similar to the risk of women in the general population.

In our Spring 2007 newsletter, we reviewed a paper that questioned the cancer risk in women who test as true negatives. Many experts on our advisory board expressed concerns regarding the study design and analysis, and felt that recommendations for counseling BRCA-negative women should not be changed based on this study.

The issue recently gained media attention when the same researchers reported similar conclusions from their latest small study. Following 238 first-degree relatives of BRCA2 carriers who tested negative for the mutation, researchers found 11 more cases of breast cancer than they would expect in the general population. First-degree relatives of BRCA1 mutation carriers who tested negative did not have a significant increase in risk when compared to the general population, although three more cases of breast cancer developed than would be expected for average-risk women.

In contrast, four separate studies published since 2007 have shown that women who test as true negatives for a familial BRCA mutation are not at significantly increased risk for breast cancer. These studies—which all support the current counseling practice for women who test true negative for a familial BRCA mutation—did not receive as much media attention as the recent study that challenges current practice.

How can several studies produce different results? The lead author of one of these studies, Dr. Allison Kurian of Stanford University School of Medicine, notes that both of the studies that found an increase in breast cancer rates for BRCA-negative family members involved families who were enrolled at a cancer genetics clinic; these women were likely to have a strong history of breast or ovarian cancer and may have had other risk factors in common with their relatives. Studies of women with BRCA mutations who receive care in more of a “real world setting” outside of high-risk clinics provide an assessment of cancer risk that is likely to apply to a broader population of families with BRCA mutations.

What does this mean for the relatives of BRCA1 or BRCA2 carriers who have tested negative for the mutation that runs in their families? Experts still believe that most relatives of BRCA1 or BRCA2 mutation carriers who test true negative are not at significantly heightened risk of breast cancer.

This study and the subsequent media attention highlight the importance of turning to a credible source of information rather than the media for information that affects health care decisions. Unfortunately, sometimes the popular press emphasizes more provocative and controversial research findings, and not all media outlets consult multiple experts to assure that their coverage is balanced and relevant. FORCE works with our Scientific Advisory Board to help translate the latest research findings into credible information. More importantly, people should consult with experts who have advanced training in cancer genetics before and after genetic testing in order to understand how genetic test results affect their personal cancer risk.

“...most relatives of BRCA1 or BRCA2 mutation carriers who test true negative are not at significantly heightened risk of breast cancer.”
How Does Patient-Centered Outcomes Research Help the HBOC Community?
People with HBOC must make important health care decisions in the face of research and knowledge gaps. Although strides have been made in HBOC research, FORCE is contacted daily by constituents who are interested in answers to questions such as:
- Will my health and quality of life be improved or harmed by taking hormone replacement?
- Are certain treatments better or more harmful for people with hereditary cancers?
- Which factors affect satisfaction with a particular type of breast reconstruction?

We will use a series of surveys, polls, and needs assessments, what we call Generator and Percolator (GAP) tools, to capture our community's health inquiries, refine and process them into research questions, and answer them through our research registry.

How People Can Participate
FORCE members may participate in the ABOUT Network in several ways. Our "generator" process starts at the community level where we will perform needs assessments, collect people's real-world health experiences, and conduct polls and surveys to determine the most important health care questions for people facing HBOC. People can participate by joining FORCE's mailing list or closed Facebook group and responding to our polls, surveys, and queries.

Those who wish to make a greater contribution to research can join our ABOUT research registry through an online portal at www.aboutnetwork.org. Participants will be asked to read and agree to a consent form, provide their preferences regarding the use of their secure data in future research, and answer a questionnaire about their health and outcomes. The information shared confidentially through the registry will be used to conduct patient-centered outcomes research. We will also offer people the opportunity to help us “Free the Data” by anonymously sharing their BRCA test results. Read our sidebar for more information.

As a research network governed by and for the HBOC community, ABOUT needs passionate and committed volunteers for our steering committee and task forces. No experience is needed, but people who are interested in a leadership role must complete training by webinar through our FORCE Research Advocate Training (FRAT) program and an application demonstrating their commitment to HBOC research. Contact Lisa Schlager at lisas@facingourrisk.org for more information.

Partner Organizations
We are partnering with other organizations to achieve our enrollment goals, build an inclusive governance structure, and assure diversity and representativeness in all aspects of the ABOUT Network. Our partners will help us promote research opportunities to their membership, assess the information and resource needs of their constituents, and participate on the ABOUT Network Steering Committee. Our partners include:
- Black Women's Health Imperative
- Ovarian Cancer National Alliance
- Sisters Network®
- Young Survival Coalition

Uncertain or Negative Results
of these genes might affect cancer risk, and in whom. Genetics experts can help patients understand how their unique genetic profile affects their cancer risk and the steps they can take to lower their risk of developing cancer and increase their chances of survival.

FORCE is dedicated to helping individuals and families who face hereditary breast and ovarian cancer. We are developing new resources to help families who test positive for mutations in genes other than BRCA1 or BRCA2 to understand their risk.

"Free the Data"—Undoing the Damage Caused by Gene Patents
by Lisa Schlager and Sue Friedman

About 3-7% of BRCA tests return with an inconclusive VUS result. The National Institutes of Health (NIH) sponsors a large database known as the Breast Information Core (BIC) for scientists to report the different variations in BRCA genes to try to unravel what they mean for cancer risk. Unfortunately, gene patents stifled progress in VUS interpretation. Myriad Genetics Laboratories held a monopoly on BRCA gene testing until 2013, when the U.S. Supreme Court ruled against gene patenting, allowing other laboratories to perform BRCA testing. The ruling, however, did not erase the negative impact of "data-hoarding." The Genomics Law Report states that Myriad stopped contributing data to BIC in favor of building a private database to retain competitive advantage over other testing companies. This strategy has hurt BRCA testing interpretation and research.

In response to this issue, the NIH launched ClinVar, a public database that collects data for all hereditary disease gene variants and can be freely accessed by researchers, consumers, and biotechnical companies. ClinVar will enable researchers to study variants, assess their significance, and facilitate medical discoveries. All information is de-identified to ensure anonymity.

The “Free the Data” movement encourages people to share their genetic test results anonymously in ClinVar. Through the ABOUT Network, FORCE and the University of South Florida are providing people with a simple way to upload their BRCA test results (with all identification removed) into ClinVar. Visit the secure website at www.freethedata.us to contribute your lab report for the benefit of the community and help us free the data.

Lisa Schlager is the Vice President of Community Affairs and Public Policy for FORCE. Based in the Washington, D.C. area, she represents the HBOC community in the legislative, regulatory and research arenas.
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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 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.

Help FORCE Go Green

Want to save some trees? Help FORCE save dollars? To receive an electronic version of this newsletter rather than a print copy e-mail us at newsletter@facingourrisk.org. Include your name and city and state in the e-mail.

FORCE to Testify to FDA in Favor of New PARP Inhibitor Approval

On June 25, the Oncologic Drugs Advisory Committee (ODAC) of the FDA will discuss AstraZeneca Pharmaceuticals' new drug application for olaparib (a PARP inhibitor) capsules as maintenance treatment of patients with platinum-sensitive relapsed ovarian cancer who have completed chemotherapy. The public meeting will take place at the FDA offices outside of Washington, D.C. PARP inhibitors were developed specifically for the treatment of cancers associated with a BRCA genetic mutation.

FORCE has been a strong proponent of PARP inhibitor research, and we will present oral commentary supporting approval of this application. We are hopeful that olaparib will be approved as a new agent for women fighting hereditary ovarian cancer.

Join Team FORCE

Get ready to get fit!

Put your training, passion, and commitment to fitness to work for a good cause: raising funds for FORCE.

Team FORCE is a community of athletes and fitness enthusiasts dedicated to supporting the hereditary breast and ovarian cancer community. These women and men commit their training and participation in races, marathons and other athletic events to raise much-needed funds for FORCE.

Team FORCE provides a great opportunity to have a positive impact on FORCE's ability to fulfill our mission by leveraging your personal fitness efforts. Visit facingourrisk.org/teamforce to join Team FORCE.