Prevention Matters

| A FOX CHASE CANCER CENTER RISK ASSESSMENT PROGRAM PUBLICATION | SPRING/SUMMER 2021

IMPORTANCE OF SHARING POSITIVE GENETIC TESTING RESULTS WITH FAMILY

Interview with Yelena Glikman, a Risk Assessment Program participant

How did you come to the Risk Assessment Program at Fox Chase?

It was just a total accident, really. When I visited my GYN office, we were discussing that my mom had a breast cancer when she was older. So, my doctor decided to order genetic testing to rule out some things. Knowing my family history of cancer, she ordered a genetic testing panel that looked at genes that increase the risk for different types of cancer. My doctor explained this test to me, but I didn't really pay attention, and I forgot all about it. She called me in a month with the positive test results. She was calm and so solid. My doctor is much younger than me, but she acted like a very strict mother. She spoke with me on the phone explaining what my next steps should be. She told me to write everything down. First, she told me to contact Fox Chase to see a genetic counselor who will explain my genetic test results and make recommendations for screening for Lynch syndrome. She told me to call her in a few weeks to let her know I scheduled my appointment. She was very persistent, and it worked because if she did not push me, I would still be researching Lynch syndrome. She kind of started this whole wheel turning.

I give 100% credit to Dr. Valerie Rabinovich, because if it wasn't for her, I wouldn't be giving this interview and my family members would not have come to Fox Chase for their genetic testing.

What did the results of genetic testing mean to you?

I was really scared because almost every one of my family members over age 55 have had a cancer diagnosis, and even some of my younger family members are developing cancer. So that was really terrifying. The more I learned about it, the more I realized that knowing I have Lynch syndrome is sort of a blessing in disguise, because there's so much you can do to prevent cancer. At this point, the way I see it, people with Lynch syndrome have an advantage, which probably sounds wrong, but they have an opportunity to have more screening that will be covered by insurance. I do not feel guilty, but I feel good for myself and for my family.

You have referred many family members to our program. Why did you feel it was important to inform your family?

I have a strong family history of cancer on my paternal side both in young and older members. The chances of them having Lynch syndrome is very high. I knew they must be screened to save their lives.

What methods have you used to inform your family?

Okay, not conventional methods. Five years ago one of my cousins had colon cancer. We had family members with cancer before, but she was the first one who tested positive for Lynch. During a family gathering she told us about the gene, she even probably mentioned Lynch syndrome and told us to call her for additional information. The response from my family was absolutely zero. So once I had my genetic results, I remembered that she did tell us something about Lynch syndrome, but for some reason we all ignored her and continued with our lives. Of course we felt sorry for her, but I guess no one thought that it can happen to us.

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FOX CHASE CANCER CENTER
TEMPLE HEALTH

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IMPORTANCE OF SHARING POSITIVE GENETIC TESTING RESULTS WITH FAMILY *Continued from Cover*

I made a list of all the family members that I could remember on my father's side and I called everybody. It took me probably a week because I spent half an hour to an hour on the phone with each one of them. I knew I was not going to succeed with a few of the men in my family, so I needed a different approach. So I spoke to their wives or mothers-in-law, and it worked. And of course, I was very, very forceful.
I remember telling one of my younger family members: "Don't talk to me unless you have an appointment". I would rather her hate me for making her go and waste her day for the counseling appointment [she lives far], than knowing that something bad happened to her.

I was forceful and persistent. And I wasn't afraid to frighten them if needed: "If you know your chance of getting cancer is greater, take an opportunity to get yourself checked."

I gathered all the necessary information for them: Risk Assessment Program's phone number, who to speak with, and how to get there. I sent everything to them by email or text, and each person had to confirm that they received it. That made it a lot easier because all they had to do is click on the phone number and call to make an appointment. I think that also helped.

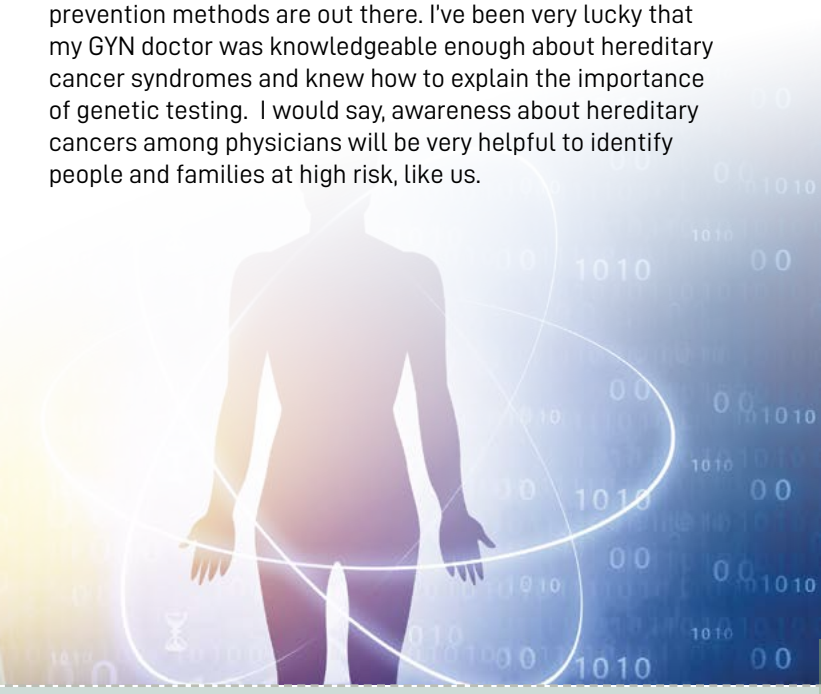
Did you have any reservations informing some of the family members?
No. Why would I? I'm not close to all my family members, and with some I have differences, but I don't want them dead, I want them to live. So there were no reservations just because we don't associate or talk. We're talking about people's lives, not personal feelings. So yeah, I picked up the phone. If it was for something else, I wouldn't pick up the phone. But for that, yes.

Were there any unsuccessful attempts?
Only one, but I'm working on this person together with another family member. I'm not losing hope.

What advice can you give others who are facing similar situation of informing family members about positive genetic testing results?
Just take your time and call or show up at their doorstep and knock. Don't take 'no' for an answer, and give them all the information. That's going to make it a lot easier for them to push the button to make that call. The hardest thing is to pick up the phone to make that call, because it can be very scary to think about 'What if I have it? What's going to happen then?' Also, it has to be a private conversation, one-on-one or through another family member who has more influence on this person. They may hate you for that, but it has to be done. That was my way, and that worked for my family, every one of them.

Do you think your family members will follow doctor's recommendations for cancer prevention?
I don't even have a slightest doubt; once they know they have it, they would do exactly what they are told to do. Once you know you have Lynch syndrome, it's kind of a scary thing. You are going to get yourself checked because you know what, it is a survival instinct, self-preservation. We all want to live. Most people want to live regardless of their age, or health condition. Once you know you have a positive test result, you are going to follow up. Oh yeah, I have no doubts.

What improvement would you like to see in Lynch syndrome screening and prevention in the next five years?
I am not a doctor, so I don't really know what the emerging prevention methods are out there. I've been very lucky that my GYN doctor was knowledgeable enough about hereditary cancer syndromes and knew how to explain the importance of genetic testing. I would say, awareness about hereditary cancers among physicians will be very helpful to identify people and families at high risk, like us.



WELCOME ABOARD FRANK INGRAM

Frank Ingram is our newest addition to the team, joining as an Administrative Specialist. He will serve as direct support to Dr. Obeid and Dr. Whitaker, as well as administrative support for the department. Frank is a Lincoln Technical Institute graduate with a degree in Medical Assisting and Administrative Technology.

Before joining Clinical Genetics, he worked as an Administrative Lead in the Emergency Trauma Center for Abington-Jefferson Health, where he handled high-acuity patient admission and coordinated medical consultation. Frank is looking forward to continuing in his new role, working in an environment where he can help to further bring excellent medical care to patients in need.

Researchers Awarded Grant to Study Use of Lipitor in Patients with Lynch Syndrome

Margie L. Clapper, PhD, co-leader of Fox Chase Cancer Center's Cancer Prevention and Control Program, has been awarded a grant by the Prevent Cancer Foundation to investigate the use of atorvastatin, also known by the brand name Lipitor, to prevent cancer in patients with Lynch syndrome. Clapper will be working with Michael J. Hall, MD, MS, co-leader of Fox Chase's Cancer Prevention and Control Program, on the project.

Lynch syndrome is an inherited disorder that increases a patient's risk of multiple types of cancer. Colorectal cancer is one of the most common in patients with this syndrome, with a lifetime risk of up to 80% in those with the genetic mutation.

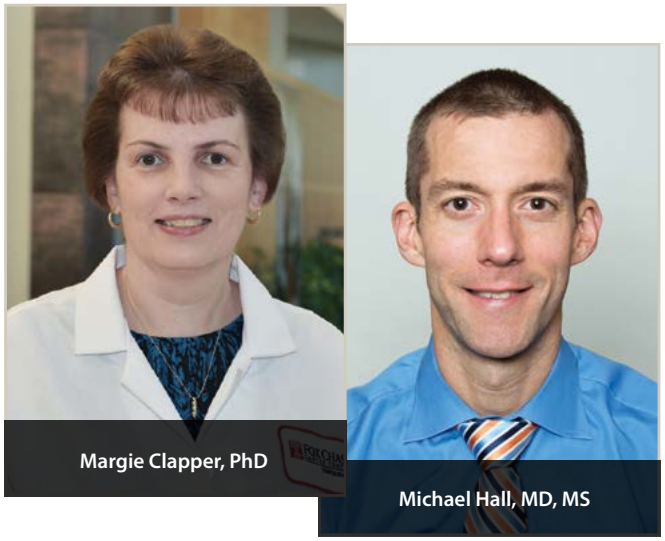
"Many of these folks have lived through years of seeing parents and siblings develop one and sometimes many cancers, and this is terrifying," said Hall. "If a once-a-day common medication like atorvastatin can help lower risk by even 20% or 30%, that's well worth it for most of these folks."

Currently the only cancer prevention regimen available to Lynch syndrome patients involves taking high doses of aspirin on a daily basis. However, in some individuals it may cause high-risk side effects. Clapper and Hall believe atorvastatin can be a safer option.

Their study began with animal-based colon cancer research in Clapper's lab.

In mice that were polyp-free, atorvastatin showed a chemopreventive, antitumor effect. If the animal had a polyp, atorvastatin was only effective when combined with a nonsteroidal anti-inflammatory agent.

To advance this research and see whether atorvastatin with or without aspirin could help to prevent colon cancer in humans, Clapper has joined forces with Hall, who treats a large Lynch syndrome population.



This study, "Impact of Atorvastatin with or without Aspirin on Colorectal Biomarkers in Patients with Lynch Syndrome: A Pilot Study," is currently in progress, with nearly 60% of the target population already enrolled. Funds will be used to assess the effectiveness of the drugs in colon tissue samples.

The resulting data are expected to accelerate the early stage development of a novel preventive option for patients who face a very high lifetime risk of colorectal cancer. The study's goal is closely aligned with the Prevent Cancer Foundation's vision to "Stop Cancer Before It Starts" using primary and secondary prevention strategies.

We would like to thank all participants who took part in this study! We truly appreciate your time, efforts, and support of our research!

We are still enrolling participants, please call **Yana Chertock** at **215-214-3216** if you are interested in this study.

Germline Mutations in ATM and Cancer Risk

Germline mutations in the ATM (Ataxia Telangiectasia Mutated) gene are relatively common, but the severity of risk is still unclear. A recent paper published by Dr. Michael Hall and researchers from Stanford University, CA estimated ATM cancer risk independent of (not related to) family cancer history in 4, 607 patients who tested positive for an ATM mutation on the hereditary cancer panel between 2013 and 2019.

Moderate-to-high risks for pancreatic, prostate, gastric, and invasive ductal breast cancers were found for ATM positive carriers. A specific mutation in ATM gene called c.7271T>G was associated with a three to four-fold increased risk for invasive ductal breast cancer than other variants. Low-to-moderate risks were seen for ductal carcinoma in situ, male breast cancer, ovarian cancer, colorectal cancer, and melanoma.

While professional society guidelines support that people who carry ATM mutation are eligible for increased breast and pancreatic cancer screening, increased screening for prostate and gastric cancer may also be warranted.

Read full article: **https://pubmed.ncbi.nlm.nih.gov/33509806/**

The Sharon Schwartz Oncofertility Program is established in memory of our dear colleague and friend, Sharon Schwartz

It is with great sadness that we inform our readers of the passing of our cherished colleague Sharon Schwartz, MSN, CRNP (1970-2020) who passed away on January 31, 2020 after an 18-month battle with cancer. Sharon has been part of the Gynecologic Oncology practice at Fox Chase Cancer Center since 2006 and has been a beloved member of the Risk Assessment Program since 2014.


Sharon Schwartz, Mary Daly, MD and Elias Obeid, MD

Many patients first came to know Sharon as their gynecologic nurse practitioner while others met her as their Risk Assessment Program clinical provider. Sharon was a well-loved clinician who provided kind, empathetic, and expert care to her patients. Not only was Sharon's hard work and dedication to Fox Chase admired by her colleagues and patients, but her personal warm character instilled hope and happiness to everyone around her. Her genuine smile would bring comfort to staff and patients alike. The Risk Assessment Program staff was so fortunate to have had the opportunity to work by her side these past six years.

Sharon is survived by a loving family including her husband and three beautiful children. She was a passionate Eagles fan as well as an avid supporter of her children's athletic events. The Advanced Practice Clinician Committee at Fox Chase recently developed an annual award in her honor to recognize an Advanced Practice Clinician for outstanding contributions to Fox Chase Cancer Center.

Among Sharon's many career achievements, her most valued legacy was the establishment of the Oncofertility Program at Fox Chase Cancer Center. This program provides consult for young patients who may have fertility issues caused by cancer treatment. Members of the Oncofertility team provide counseling and information to patients, coordinate appropriate referrals to specialists, and provide follow-up to patients and their referring physicians.

The program has been renamed in Sharon's honor to the **Sharon Schwartz Oncofertility Program**. The program is facilitated through the volunteer efforts of nurses and Advanced Practice Clinicians at the hospital. Sharon requested donations to the program, at her passing, to help fund small grants for patients who could not afford the total cost of fertility preservation services. Donations in her honor would be gratefully accepted and can be made out to **Fox Chase Cancer Center, Institutional Advancement, Oncofertility Program, 333 Cottman Avenue, Philadelphia, PA 19111**.

Kristen Whitaker Receives Grant from V Foundation for Cancer Research

Kristen D. Whitaker, MD, MS, assistant professor in the Department of Clinical Genetics at Fox Chase Cancer Center, recently received a grant from the V Foundation for Cancer Research to study ways of improving diversity in clinical cancer trials. The grant was funded by Hooters of America, LLC.

The V Foundation was founded by famed college basketball coach Jim Valvano and ESPN to fund cancer research and accelerate efforts toward potential treatments. The Foundation has awarded more than $260 million in cancer research grants nationwide. Whitaker was awarded a one-year grant for her work.

"My project is specifically targeted toward African American patients with breast cancer and how we can improve their involvement in clinical trials," said Whitaker. "Currently, only about 2.5% of cancer patients participate in any type of clinical trial."

Dr. Whitaker said this is an important endeavor because clinical trials play a critical role in terms of determining the efficacy of new treatments, as well as their safety profiles. The efficacy of drugs and side effects can also differ in various racial groups.

"With this in mind, it's very important that clinical trials have diverse racial representation", Dr. Whitaker said.

Whitaker's proposal involves randomizing patients into two groups that have slightly different interventions based on an educational brochure.

She will compare outcomes of educational intervention based on a standard clinical trial educational handout and a "culturally tailored" educational brochure that highlights unique issues or concerns that have previously been reported by Black patients related to clinical trial enrollment.

"One thing we know for sure that Black patients report frequently that one reason they don't participate in clinical trials is due to distrust of healthcare providers and the healthcare system. We also know that they are more likely to report concerns about potential harm from being in a clinical trial," said Whitaker.

"As someone who is well aware of the racial disparity in breast cancer mortality between Black and white patients, I think this study is really important to conduct," said Whitaker. "I really see this as a launching point for assessing the efficacy of this intervention in larger study populations in the future."

BEYOND MULTI-GENE PANEL TESTING. WHAT'S COMING DOWN THE LINE?

By Catie Neumann, MS, LCGC, a genetic counselor

It has been almost a decade since we started offering multi-gene panel testing to our patients. Multigene panel testing is a type of genetic testing that looks for mutations in many genes at once. This is different from single-gene testing, which looks for a mutation in a specific gene, for example in BRCA1 or BRCA2.

With advances in sequencing technologies, we have a better understanding of cancer genetics processes, and the application of new methods to studying cancer holds great promise for developing important breakthroughs in cancer treatment and prevention. So, what is next?

RNA Testing

RNA is now very much a part of our public vocabulary because of the mRNA vaccines for COVID-19.

DNA stores our genetic information, whereas RNA acts as a messenger to get this information to the parts of our cell that make proteins. Typical genetic testing for hereditary cancer is done on DNA rather than RNA.

RNA has not been routinely tested for patients undergoing hereditary cancer testing, but it has had some clinical utility to help clarify certain types of uncertain results. It can also potentially detect mutations that may have been missed in DNA testing alone. In the past, this was only done on select patients who the laboratory thought it would be helpful to clarify an uncertain result. Those were selected by the laboratory and done on a research basis. But now there is a laboratory that is performing paired RNA and DNA genetic testing at the same time. It requires an extra tube of blood drawn. This paired RNA and DNA testing has only been around for a year. But the data do look promising that this could potentially help clarify results in a subset of patients.

Paired Tumor/Germline Testing

Oncologists may order genetic testing on a patient's tumor to help look for potential target therapies. It's important to distinguish the difference between tumor genetic testing and what we call germline, or inherited, genetic testing. Tumor testing looks for mutations that are present in the tumor only. However, if someone also has an inherited mutation (one we would find in the blood or saliva), that mutation may also be present in the tumor as well.

For some patients, we look through tumor testing results to see if there are any mutations that might be suspicious for an inherited result, and then we would need to do further testing to confirm by doing blood or saliva testing. If the mutation is only present in the tumor, it is not something that you can pass on. Instead of doing two separate tests, some companies are now offering paired tumor and germline (hereditary) testing to be done at the same time.

Polygenic Risk Score

A polygenic risk score is a percentage risk for a cancer based on variations in the "spelling" of multiple genes. Each of these spelling variations alone would not drastically change cancer risk like finding a mutation in BRCA or Lynch syndrome gene would. The laboratory creates the risk score by adding together all the variations that increase risk and variations that decrease cancer risk. Some laboratories will also use personal and family history to contribute to the risk score.

It is important to note that although some laboratories are reporting this information on hereditary genetic test reports, these scores are not yet used to make clinical management decisions. However, this may change over time.

CANCER RISK ASSESSMENT SERVICES BEING OFFERED AT TEMPLE

The Fox Chase Clinical Genetics counseling services are now being offered at Temple University Hospital (TUH) Main Campus, beginning in March 2021. Fox Chase genetic counselor, Hannah Campbell, MS, LCGC, will see patients for cancer genetic counseling and testing at TUH Main Campus on Broad Street.

The Cancer Prevention and Risk Assessment services will also be expanding to TUH Main Campus. A monthly High-risk Breast/Ovarian Cancer Clinic, led by Kristen Whitaker, MD, MS, and a monthly High-risk Prostate Cancer Clinic, led by Elias Obeid, MD, MPH, will expand the cancer related services within the health system.

Interested patients may call the Fox Chase Risk Assessment Program at 877-627-9684 to speak with an intake coordinator about personal health history and family history of cancer. After the intake process, an appointment will be scheduled at Temple main campus for genetic counseling or high-risk clinics by Temple's central scheduling team.

MAN 2 MAN

REDUCED PSA SCREENING MAY BE ASSOCIATED WITH RISE IN METASTATIC PROSTATE CANCER IN THE US

A recent abstract at the 2021 Genitourinary Cancers Symposium at the American Society of Clinical Oncology (ASCO), looked to see if reductions in prostate- specific antigen (PSA) screening has contributed to increased metastatic prostate cancer in the US. The US Preventative Services Task Force (USPSTF) did not recommend PSA screening in 2008 and 2012.

Researchers looked at incidences of metastatic prostate cancer at diagnosis per 100,000 men for each state between 2002-2016. The percent of men greater than age 40 who reported ever having PSA screening was dissimilar between states (range 40.1%-70.3%) as well as the incidence of metastatic prostate cancer at diagnosis (range 3.3 to 14.3 per 100,000). Between 2008-2016 the mean percentage of men screened with PSA test decreased (61.8% to 50.5%) and the mean incidence of metastatic prostate cancer at diagnosis increased (6.4 to 9.0 per 100,000). These results indicated that states with lower PSA screening had larger increases in metastatic prostate cancer at diagnosis.

This study provides evidence that reduced PSA screening may explain the recent increase in metastatic prostate cancer at diagnosis in the United States.

In 2018, the USPSTF revised the recommendation for men age 55-69. This revision states that patients and doctors should consider the benefits and risks of PSA screening based on family history, race/ethnicity, patient medical conditions, patient values about benefit/risk of screening and treatment outcomes and other health needs of the patient.

Read abstract:
https://meetinglibrary.asco.org/record/195181/abstract

Final Recommendation Statement: Screening for Prostate Cancer:
www.uspreventiveservicestaskforce.org/uspstf/announcements/final-recommendation-statement-screening-prostate-cancer

SUN SAFETY TIPS FOR MEN

Men, especially those with lighter skin, are more likely than anybody else to get skin cancer, including melanoma—the deadliest kind of skin cancer.

When you think about sun protection, you might think about a day at the beach. But over your lifetime, you get sun exposure doing everyday things like biking, working, running, or even mowing the lawn. Sun exposure is the main source of ultraviolet (UV) rays, which can cause skin cancer. And UV exposure adds up over time, increasing your risk of developing skin cancer.

Skin cancer is the most common cancer in the United States. Every year, nearly 5 million people are treated for skin cancer, at a cost of about $8 billion. Melanoma causes around 8,000 deaths per year in the U.S.

Men tend to get more sun exposure than women. Men spend more time outside over their lifetimes than women, and they're more likely to work outdoors than women. Women's personal care products, like moisturizer and makeup, often contain sunscreen, while many products for men don't.

About one-third of U.S. adults get sunburned each year. Sunburn, which can increase your risk of getting skin cancer, is common among white men, young adults, and men who tan indoors. When outside on a sunny day for more than an hour, only about 14% of men use sunscreen on both their face and other exposed skin.

Easy Ways to Protect Yourself

- Long-sleeved shirts, pants, and a wide-brimmed hat offer the best protection. If you're wearing a baseball cap or short-sleeved shirt, make sure to put sunscreen on your ears, neck, and arms.
- Stay in the shade as much as possible between 10 a.m. and 4 p.m., which are peak times for sunlight.
- Use a broad spectrum sunscreen of at least SPF 15 on any exposed skin, and don't forget to re-apply it every two hours, as well as after swimming, sweating, or toweling off.
- If you work outdoors, ask about sun protection at your job, like wearing sun-protective clothing.
- Avoid indoor tanning.

Source: https://www.cdc.gov/cancer/skin/

ASK THE GENETIC COUNSELOR

Q: I HAVE A KNOWN MUTATION IN MY FAMILY. SHOULD I JUST GET TESTING FOR THAT MUTATION OR SHOULD I GO FOR THE LARGER PANEL TEST?

Catie Neumann, a genetic counselor: When there is a known mutation in the family, there is the option to pursue single site testing, meaning the laboratory would only look for the mutation that has already been identified in family members. There is also the option to pursue multigene panel testing which means testing for multiple genes at the same time. While rare, multigene panel testing can identify an additional gene mutation that had not previously been found in the family. To decide whether or not a multigene panel is appropriate when there is a known mutation in the family, there are a few questions we need to ask.

First, is there a significant family history of cancer coming from the side of the family that does not carry the mutation? We receive 50% of our genetic information from each parent so it is possible that a mutation could be coming from the other side of the family. Second, are there cancers in the family not explained by the mutation? Different gene mutations are associated with specific cancer risks. If there are cancers in the family that are not associated with the gene mutation in the family and are suspicious for hereditary cancer (young age at diagnosis, rare cancer, etc), then a panel may be appropriate.

Additionally, have other family members undergone panel based testing or single site testing? If all the family members who were diagnosed with cancer have undergone multigene panel testing or if both of your parents have undergone multigene panel testing, the likelihood of finding another mutation is decreased.

Finally, will your insurance cover panel testing? If there is a known mutation in the family, some insurances will only pay for single site testing rather than multigene panel testing. If a patient still wants to pursue panel testing even though insurance will not pay for a panel, there are out of pocket options that range from $50-$250.

PHYSICAL ACTIVITY AND REDUCED BREAST CANCER RISK IN ADULT WOMEN AT HIGH RISK FOR BREAST CANCER

Women at higher risk for breast cancer either because of family history or a genetic mutation often ask about non-surgical strategies to reduce their cancer risk. Physical activity has long been associated with lower breast cancer risk. However, for women with a familial or genetic risk for breast cancer is it still unknown how physical activity could affect their cancer risk.

Researchers from our Breast Cancer Family Registry (BCFR) team used self or relative reported questionnaire data from our participants to look at the association of recreational physical activity, at baseline (first entering the study) and during adolescence, with breast cancer risk. They examined whether associations were modified by underlying familial risk (based on pedigree data) or by genetic risk (BRCA1 or BRCA2 mutation). The final sample analyzed for the study was 15,550 women from 6,503 families, including 659 BRCA1 and 526 BRCA2 mutation carriers.

Evidence suggests that recreational physical activity during adulthood is associated with lower breast cancer risk. Specifically, the researchers found that attaining at least 2.7 hours of moderate or 1.5 hours of strenuous physical activity per week was associated with a 20% lower breast cancer risk. There was no association with physical activity during adolescence. They did not find evidence that the association of baseline recreational physical activity with breast cancer risk is changed by familial risk or by BRCA mutation status.

The study provides further support for an association between recreational physical activity in adulthood and breast cancer risk and suggests that even a modest level of physical activity in adulthood is associated with reduced breast cancer risk. In addition, this association exists for women at high familial and genetic risk. Therefore, physical activity could be an effective prevention strategy for all women, especially for women at higher than average risk of breast cancer.

Read article:
https://pubmed.ncbi.nlm.nih.gov/31578201/

Prevention *matters*

The Department of Clinical Genetics offers one of the most comprehensive risk assessment programs in the Philadelphia region. It encompasses all of Fox Chase Cancer Center's clinical services for people at risk for cancer, as well as innovative research in the areas of cancer prevention and genetics.

CONTACT THE RISK ASSESSMENT PROGRAM:

1-877-627-9684 | foxchase.org/rap | rapinfo@fccc.edu

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Understanding Hereditary Risk: A Virtual Event for Patients, Families, and Friends of FCCC

Hosted by the Department of Clinical Genetics at
Fox Chase Cancer Center via Fox Chase Cancer Center
Facebook Page *(you do not need an account to view)*

Tuesday , June 22, 2021
6:30pm-8:00pm

For more information or to register, please go to:
www.FoxChase.Org/HereditaryCancers2021

FOX CHASE CANCER CENTER
Department of Clinical Genetics
Risk Assessment Program
FoxChase.org/RAP

Please register online by June 1 to receive a program packet.

Editors: Yana Chertock, Lisa Bealin, Joann Sicilia and Nicole Ventriglia
Designed by **4545 Creative**

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