

Prevention Matters

| A FOX CHASE CANCER CENTER RISK ASSESSMENT PROGRAM PUBLICATION | FALL/WINTER 2020

Department of Clinical Genetics: Our Research at a Glance

Clinical research is research in which people, or data or samples of tissue from people, are studied to understand health and disease. Clinical research helps find new and better ways to detect, diagnose, treat, and prevent disease.

When people volunteer to take part in clinical research, they help doctors and researchers learn more about disease and improve health care for people in the future. In some way, each of us has benefited from people willing to participate in clinical research.

There are many types of clinical research studies; in the Department of Clinical Genetics we conduct several types of research, each with a specific purpose:

Prevention Trials study ways to reduce the risk of getting cancer. Most prevention trials involve healthy volunteers who have been identified as at high risk for developing cancer. Different kinds of prevention research may study medicines, vitamins, vaccines, or lifestyle change. In the study, *Impact of Atorvastatin and Aspirin on Colorectal Biomarkers in Patients with Lynch Syndrome*, we investigate how common medications such as aspirin and lipitor can prevent colorectal polyps and reduce risk of developing colorectal cancers in individuals with Lynch syndrome, a syndrome characterized by high rates of colorectal cancer.

Genetics Studies examine how genetic makeup can affect detection, diagnosis or response to cancer treatment. In our recently approved study, *Germline genetic testing for hereditary cancer risk in patients with biliary tract cancer and never smokers with NSCLC*, we'll conduct genetic testing in patients with biliary tract cancer and never smoking lung cancer to increase our knowledge regarding hereditary cancer risk among these under-tested populations and their families.

Screening Trials study ways to better detect cancer, especially in the early stages. *Prostate Risk Assessment Program (PRAP)* is a research and clinical program for men at high risk for prostate cancer. Men have a clinic visit once a year that includes a PSA (Prostate-Specific Antigen) test and DRE (digital rectal exam) to screen for prostate cancer. Men provide family and health history, lifestyle information, and a blood sample for researchers to study this population.



Behavioral Studies aim to study and/or change behaviors; for example, increase cancer screening or reduce sun exposure. Studies may focus on cancer prevention, education, early detection, treatment, and survivorship. The *E-IMPART* study sponsored by the American Cancer Society explores the perceptions of genetic risk in African American cancer patients to develop an online education tool that will help patients make an informed decision regarding testing tumors for genetic changes.

Epidemiology or Population-Based Studies look at information collected from large groups of people to help understand the patterns, causes, and control of cancer in the groups being studied.

The Risk Assessment Program (RAP) Registry is a research study for people who have a higher than average risk of cancer. We collect information, such as family and health history, risk factors, lifestyle information, and blood sample of large numbers of people. Since 1991, we enrolled more than 11,000 healthy volunteers, patients, and family members. The data and specimens provide an ongoing source of valuable information for researchers to study ways to prevent, diagnose, and treat cancer now, and in the future.

Another example is the *Breast Cancer Family Registry (BCFR)*, an international consortium established as a resource for research on the epidemiologic, clinical, and genetic aspects of breast cancer funded by the National Cancer

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Institute (NCI). Six sites, including the Philadelphia site, have collaborated to enroll more than 12,000 families at high risk for breast cancer into a family-based registry. Currently, the registry is working on the study, *Creation of a Young Women's Cohort for the Breast Cancer Family Registry*. This study focuses on consenting daughters ages 18 to 40 from our currently participating BCFR families. The ultimate goal is to create a resource for future research on the biological factors and exposures experienced by women ages 18-40 that may be related to a future risk of breast cancer.

External collaborative studies. The Department of Clinical Genetics has been working together with other institutions nationwide and internationally and continuing to contribute to cancer research.

Dr. Michael Hall recently participated in the worldwide study of cancer risk for Lynch syndrome. The International Mismatch Repair Consortium was formed in 2010 and contains the major research and clinical groups in the world researching and treating Lynch syndrome. The study estimates cancer risk by geographic region, for carriers of germline mutations in DNA mismatch repair genes.

Another recent collaboration of Dr. Michael Hall with Dr. Matthew Yurgelun from Harvard Medical School, is a multi-institutional study on therapy-associated gastrointestinal polyposis in survivors of childhood and young adulthood cancers.



Dr. Mary Daly collaborates with Dr. Tim Rebbeck from Dana-Farber Cancer Institute on the study, *Assessing Personal Thresholds for Risk to Undergo Risk-Reducing Surgery*, funded by the National Institute of Health (NIH). The study is looking at how women make decisions about reducing their risk for ovarian cancer.

Dr. Elias Obeid collaborates with Professor Rosalind Eeles from The Royal Marsden Hospital and Institute of Cancer Research in the UK and other researchers from around the world on the *IMPACT study*. This study looks at men at risk for prostate cancer with and without a genetic mutation and follows them to learn more about mutations and prostate cancer risk.

We thank all the participants who have taken part in research at Fox Chase and specifically in the Department of Clinical Genetics. We continue to collect valuable data from surveys, blood samples, and specimens and share the information with other researchers and doctors around the world. The results from these studies often help doctors provide better and improved care to their patients.

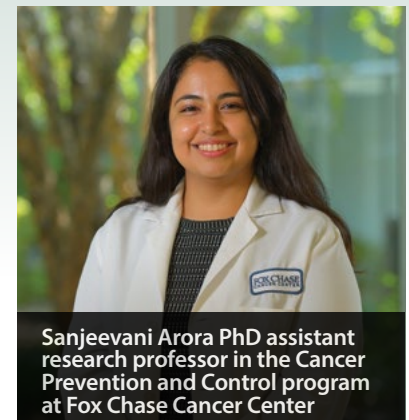
Genetic variants in early-onset renal (kidney) cancer: implications for genetic testing, cancer risk assessment, and cancer therapy

Renal cancer often develops with no signs or symptoms and is often referred to as the "silent disease". Several risk factors have been associated with renal cancer risk, and these include genetics, smoking, environment, obesity, and race. Genetics seems to play the biggest role for increased renal cancer risk.

Typically, an early-onset of disease is a trigger for genetic testing in renal cancer patients. The genes that are established in early-onset renal cancer are the following genes - VHL, MET, FLCN, TSC1, TSC2, FH, SDH, PTEN and BAP1. However, for most patients with early-onset renal cancer, a pathogenic [disease-causing] genetic change in these genes is not found. This means that many renal cancers remain genetically unexplained. More research is needed to identify additional genes that may increase renal cancer risk.

At Fox Chase we used genetic test results from 844 patients with early-onset renal cancer (<60 years old). These patients underwent genetic testing with a multi-gene cancer panel by Ambry Genetics. We report that pathogenic genetic changes were identified in multiple cancer-risk genes in patients in the study. Of these renal cancer patients with pathogenic changes, the majority of the changes were in

genes that are typically not known to increase renal cancer risk. These genes are DNA damage response and repair (DDRR) genes, and they ensure that DNA in the cells is not damaged, and thereby maintain genetic stability. We found that the most common pathogenic changes were in the following DDRR genes- CHEK2, BRCA1, BRCA2, and ATM. These genes are known to increase risk for other cancers, such as breast and ovarian cancer (BRCA genes), but have not been associated with renal cancer risk.



Sanjeevani Arora PhD assistant research professor in the Cancer Prevention and Control program at Fox Chase Cancer Center

From these data, we conclude that multi-gene cancer panel testing, including DDRR genes, may provide a more thorough risk assessment in early-onset renal cancer patients, and their families. These findings also suggest that some renal cancer patients may respond to therapies that target vulnerabilities in DDRR, such as PARP inhibitor therapy. More research is needed with larger renal cancer datasets to determine the association of certain genes and early onset renal cancer.



Importance of Continuing your Routine Cancer Prevention and Screenings During COVID-19

Regular mammograms, colonoscopies, Pap tests, prostate, lung and skin screening exams are the best way to detect cancer before it starts or at its earliest stages when the chance for successful treatment is high.

At the onset of the COVID-19 pandemic, these procedures were largely put on hold to prioritize urgent needs and reduce the risk of the spread of COVID-19 in healthcare settings. One outcome of this has been a sharp decrease in cancer screening.

More than a third of American adults have skipped scheduled cancer screenings during the pandemic, a survey by the Prevent Cancer Foundation found. Recent research has shown that new cancer diagnoses have declined since the beginning of the pandemic, possibly due to delayed cancer screenings and other routine health care appointments. It is estimated by the National Cancer Institute that reduced screening for six months due to COVID-19 and the resulting delays in diagnosis and treatment could lead to nearly 10,000 extra deaths from breast and colorectal cancer alone over the next decade.

People who are at a higher risk for developing cancer — those with a family history, a known genetic mutation, a history of polyps, or who have had an abnormal screening in the past — are strongly urged not to skip screenings. Those with average risk should talk to their doctor about the pros and cons of delaying screening.

Cancer screenings are back in full swing at Fox Chase Cancer Center. The Department of Clinical Genetics offers three high-risk screening clinics that offer long-term follow-up care for those at high risk: high-risk breast clinic, high-risk gastrointestinal clinic, and high-risk prostate clinic.



Our high- risk clinics' team of doctors and nurses help individuals and families evaluate their risk for different types of cancer and develop a healthcare plan for screening and cancer prevention. Routine clinical exams, coupled with screening, are the best means of early detection.

Cancer won't wait for the pandemic to end- and neither should screenings. That's why it's important to put preventive care back on your to-do list.

Fox Chase is determined to keep COVID-19 out of our center and is following guidelines to keep our patients safe. Please check our website for information about protective actions we take: [FOXCHASE.ORG](https://www.foxchase.org)

To schedule your appointment please call **877-627-9684** or email rapinfo@fcc.edu

Breast Cancer Family Registry Participants: If you have changed your home address, phone number or email address, please email lisa.bealin@fcc.edu with your current information. We appreciate your ongoing participation in the Registry. Thank you!



WELCOME ABOARD KATHLEEN HENDERSON, MSN, CRNP

Kathy has worked her entire career in the oncology field since obtaining her BSN degree in 1992. She received her Master's degree and Nurse Practitioner certification at the University of Pennsylvania. Throughout her career, she has valued her interactions with patients and colleagues, as well as the ongoing advancements in cancer treatment.

In 2016, Kathy began working with the breast surgery team at Fox Chase in managing benign breast conditions and breast cancer survivors. In her current role with the Department of Clinical Genetics, she evaluates high-risk patients based on their personal medical history, family history of cancer, and genetic mutations. Kathy helps to guide these patients with high-risk screening and interventions to decrease cancer risk.



Young adults are not immune from colorectal cancer

By Michael Hall, MD, MS, GI oncologist and genetic risk specialist

Healthcare providers are witnessing a disturbing trend in colorectal cancer—in recent years, more young adults under the age of 50 are being diagnosed with colorectal cancer. The recent death of Chadwick Boseman, the star of the international movie hit *Black Panther*, highlights a risk that is affecting young people much more frequently than in the past, and triggers a call for greater awareness.

While population screening for colorectal cancer starting at age 50 has led to declining rates of colorectal cancer in the US, several recent studies have found that rates of colorectal cancer among those under 50, before many people even think of screening, is on the rise. Some of these cases are due to hereditary risks, but less than 20% of cancers in patients diagnosed under 50 are hereditary. In fact, most colorectal cancers occur in people who don't have a family history or a known genetic predisposition.

What do we know about the main risk factors for colorectal cancer in young adults?

Dr. Hall: Aside from those young people who have genetic risks that we can detect through genetic testing, we actually know very little right now about what factors are leading to this increase in young onset colorectal cancer. Some experts believe this is linked to lifestyle factors like higher rates of obesity and lower rates of physical activity, while others think the cause may be an occult infectious cause, perhaps related to the microbiome of our guts. On the other hand, there are other experts who think that there has really been no change, but that we are just detecting more early onset colorectal cancers due to greater availability of colonoscopy and other tools to detect these cancers.

What are the screening recommendations for colorectal cancer?

Dr. Hall: These recommendations vary by expert group, but most US based guideline groups still recommend initiation of screening for average risk Americans at age 50, via a variety of modalities, but most often via colonoscopy. In 2018, the American Cancer Society changed their recommended age of colonoscopy start to 45 for average risk Americans based on data suggesting rising rates in young adults. This decision has been hotly debated for many reasons, not the least of which being the increased demand on limited healthcare resources without clearly defined benefits that this change will create. It should be noted however, that for several years now, some expert groups have recommended that African American persons initiate colonoscopy screening early (age 45) due to data demonstrating clearly higher rates of diagnosis and cancer-related death in this group.

What should young adults do to prevent the disease?

Dr. Hall: This is a tough question as there are no specific recommendations—but my recommendations would be:

1. have a primary care provider and see them regularly—while a routine doctors visit will not detect all early colorectal cancers through history, exam, and blood tests, it will detect some
2. get regular exercise—physical activity is one of the best cancer prevention approaches, and has been shown to be associated with a 20% lower risk of colorectal cancers.
3. Know your body and don't ignore early warning signs like blood in your stool and unexplained weight loss
4. improve your eating habits and maintain a healthy body weight—in particular, increase your fruits and vegetables, lower your red meat consumption, keep your alcohol consumption light, minimize processed foods, fast foods, and sugar-sweetened drinks, like soda—they may all taste great and be more convenient, but they are not great for your body in the long run.



Breastfeeding: A Public Health Strategy for Reducing Risk of Ovarian Cancer

By Mary Daly, MD, PhD, Director of the Risk Assessment Program

Although early-stage disease is highly curable, most ovarian cancers are diagnosed at later stages, due to a lack of effective screening. As a result, less than 50% of women survive beyond 5 years. Identifying ways to prevent ovarian cancer could dramatically change the outcome of this disease. Epidemiologic studies have shown that childbirth, oral contraceptive use, and tubal ligation (getting tubes tied) can alter the risk of ovarian cancer.

Breastfeeding has been suggested as another possible preventative measure for ovarian cancer.

A recently published study in *JAMA Oncology* analyzed 9,973 cases and 13,848 controls from 13 case-control studies to study the connection between breastfeeding and ovarian cancer. They found breastfeeding was associated with an overall 24% lower risk of ovarian cancer, adjusting for oral contraceptive use and independent of how many times women gave birth. The association was seen both for invasive and borderline ovarian tumors. The

reduction in risk was seen within as few as 1 to 3 months of breastfeeding and increased with the duration of breastfeeding. While it was greatest for more recent breastfeeding, the reduction in risk lasted for decades.

However, some questions remain. Despite decades of studies examining the connection between breastfeeding and ovarian cancer, the underlying biological mechanisms that could explain the reduction in risk are not known. The fact that just 3 months of breastfeeding can have a significant and long-lasting impact on ovarian cancer risk suggests a powerful mechanism that permanently alters the ovaries.

A leading "incessant ovulation" theory suggests that continued ovulation causes rupture and trauma to the ovaries and could lead to cancer; any interruption of ovulation, therefore, such as breastfeeding, pregnancy, or oral contraceptive use, could lower the risk of ovarian cancer. Further research is needed to clarify the mechanism(s) involved in reducing the risk of ovarian cancer



by breastfeeding. This could potentially provide different interventions for women who don't or are unable to breastfeed.

Given the lack of effective screening for ovarian cancer and its high case-fatality rate, public health efforts to overcome barriers to breastfeeding could provide a significant contribution to the prevention of ovarian cancer.

Read full article:
<https://bit.ly/33HWRNv>

Using Chemoprevention to Reduce the Risk of Breast Cancer in Women

Among women in the United States, breast cancer remains the most common cancer and is the second leading cause of cancer-related deaths. While diagnosis rates have been stable over the past 30 years, death rates have been lowered, likely due to earlier detection by broad screening and improved treatments. To help women who are at a higher risk for breast cancer, the US Preventive Services Task Force (USPSTF) recommends that doctors offer to prescribe tamoxifen, raloxifene, or aromatase inhibitors (AIs) for cancer prevention. This recommendation is based on 20 years of clinical trial research that has shown how effective chemoprevention is in lowering breast cancer risk. In all of the clinical trials, drug therapy was effective in reducing only estrogen receptor-positive breast cancers by 50%.

In order for these risk-reducing medications to be successful, doctors must understand the range of factors that would determine if chemoprevention would benefit their patient. Current risk-assessment models that include risk factors such as family history and benign breast disease, can be complex and time-consuming. Doctors also need to be able and willing to educate their patients about their risk for breast cancer and the risks and benefits of taking risk-reducing drugs to help their patient make informed decisions. This is a challenge as clinic time with patients shortens. Additionally, more data are needed on the long-term effects of AIs, while data on the benefits and risks of all of the available drugs is limited for African-American and Hispanic women. Many women are dissatisfied with and distrustful of the medical community, especially when it comes to the use of risk-reducing medications. It is estimated that more than 10 million women in the United States would be able to get tamoxifen therapy for breast cancer prevention. However, data from the National Health Interview Study in 2010 found that fewer than 1% of eligible women were taking or had taken tamoxifen or raloxifene for prevention.

New risk-assessment models may offer an opportunity to personalize benefit and risk estimates for women considering breast cancer chemoprevention. If doctors are able to accurately use these models and have helpful discussions with their patients, chemoprevention can continue to help women reduce their risk of developing breast cancer.





MAN 2 MAN



SOCIAL ENVIRONMENT CAN EFFECT PROSTATE CANCER DEVELOPMENT IN MEN AT HIGH RISK FOR PROSTATE CANCER

Men who have a family history of a prostate cancer (PCa), as well as Black men, have a 2-7 fold increased risk for PCa compared to the general population. When comparing Black and White men, Black men are more than twice as likely to be diagnosed with and die of PCa. Some studies have shown that in addition to ethnicity and family history, socioeconomic factors, including whether a person is employed, has a higher level of education or income, and the social and physical conditions of the neighborhood in which a person lives (e.g. poverty level, housing conditions, transportation access in a neighborhood), may also be related to an increased risk of a PCa diagnosis or dying from PCa.

In a new publication titled, *The effect of neighborhood social environment on prostate cancer development in Black and White men at high risk for prostate cancer*, researchers from Fox Chase looked at social environment factors from where a patient lives and their effect on the time to a prostate cancer diagnosis in White and Black Men with and without a prostate cancer family history. Data on 358 high risk men aged 35 to 69 enrolled in the Prostate Risk Assessment Program (PRAP) were analyzed in order to determine whether the addition of neighborhood factors could help identify patients at higher risk for a PCa diagnosis. This data

has the potential to become a helpful aid in clinical decisions about prostate cancer screening and surveillance. Results showed that neighborhood socioeconomic factors were associated with time to a PCa diagnosis, but they differed by race and by PCa family history. Living in neighborhoods with a higher percentage of workers who use public transportation to get to work, and in neighborhoods with more low income residents were significantly related to shorter time to PCa in White men with a PCa family history. Living in a neighborhood with a higher percentage of homeownership and unemployment were associated with shorter time to PCa diagnosis in Black men with and without a PCa family history, respectively. The study showed that for both Black and White men, living in a neighborhood with a higher percentage of significant neighborhood variables, such as unemployment, low income, home ownership, were associated with a 2-4 time greater probability of developing PCa, even if the initial PSA level was low (below 4ng/mL). Findings suggest neighborhood data (income, employment, mode of transportation) could be useful to identify high risk men affected by disparities, but future studies with a larger population are needed.

<https://journals.plos.org/plosone/article?id=10.1371/journal>

HIGHER DAILY STEP COUNT LINKED WITH LOWER ALL-CAUSE MORTALITY

In a new study, the research team from the National Cancer Institute (NCI) and the National Institute on Aging (NIA) found that higher daily step counts were associated with lower mortality risk from all causes.

"While we knew physical activity is good for you, we didn't know how many steps per day you need to take to lower your mortality risk or whether stepping at a higher intensity makes a difference," said one of the investigators of the study.

The study tracked 4,800 adults aged 40 and over using fitness trackers and phone apps between 2003 and 2006. The participants were then followed for mortality through 2015 via the National Death Index. Researchers found that:

- Taking 8,000 steps a day was linked with a 51% lower risk of death from any cause compared with taking 4,000 steps a day.
- Taking 12,000 steps a day was linked with a 65% lower risk than taking 4,000 steps a day.
- There was no significant difference in death risk based on how fast people walked, only on the number of steps they took.

The authors also found that higher step counts were associated with lower all-cause death rates among both men and women; among both younger and older adults; and among white, black,

and Mexican-American adults. Higher step counts were also associated with lower rates of death from cardiovascular disease and cancer.

These findings are consistent with current recommendations that adults should move more and sit less throughout the day. Adults who do any amount of physical activity gain some health benefits.

For even greater health benefits, adults are recommended to get at least 150 minutes of moderate-intensity physical activity per week. Being physically active has many benefits, including reducing a person's risk of obesity, heart disease, type 2 diabetes, and some cancers. And on a daily basis, it can help people feel better and sleep better.

Source: National Cancer Institute (NCI) <https://www.cancer.gov/news-events/press-releases/2020/daily-step-count-mortality>



HEALTHY RECIPE

Golden Quick Barley with Sweet Peas and Corn

For a quick and easy side dish, look no further than your pantry and freezer staples. Quick cooking barley pairs well with frozen sweet green peas and corn. Barley is a whole grain that's rich in soluble fiber, beneficial for controlling blood sugar, cholesterol and weight. It also contains beta-glucans that may help prevent inflammation and chronic diseases like cancer. Turmeric contains curcumin, a golden pigment that has antioxidant and anti-inflammatory properties.

Ingredients:

- 1 Tbsp. extra virgin olive oil
- 1 small onion, chopped
- 2 cloves garlic, minced
- 3/4 cup quick pearled barley
- 2 cups low-sodium vegetable or chicken broth
- 1 tsp. Italian seasoning
- 1/2 tsp. salt
- 1/8 tsp. ground turmeric
- 1/4 tsp. freshly ground black pepper
- 1/2 cup frozen sweet peas
- 1/2 cup frozen sweet corn
- Juice of 1/4 fresh lemon (about 1 Tbsp.)
- 1-2 Tbsp. shredded Pecorino Romano or Parmesan cheese, optional

Directions:

1. In 2-quart medium saucepan, heat oil over medium-high heat. Sauté onion until softened, about 4 minutes. Add garlic and sauté for 30 seconds. Add barley and stir 1 minute to toast.
2. Add broth, Italian seasoning, salt, turmeric and 4-5 grinds pepper. Increase heat to high and bring mixture to a boil. Reduce heat to simmer, cover and cook 15 minutes.
3. Stir in peas and corn. Cover and simmer 5 minutes. Barley mix should be slightly wet.
4. Stir in lemon juice. Sprinkle on or mix in cheese, if using, and serve immediately.

Makes 3 Servings (3/4 cups per serving).

Per serving: Per serving: 220 calories, 5 g total fat (1 g saturated fat, 0 g trans-fat), 5 mg cholesterol, 40 g carbohydrates, 7 g protein, 8 g dietary fiber, 420 mg sodium, 3 g sugar, 0 g added sugar.



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ALCOHOL AND CANCER: WHAT ARE THE RISKS?

There is no doubt: "Alcohol is a cause of cancer," said Rishi Jain, MD, MS, DABOM, a medical oncologist at Fox Chase Cancer Center. "An estimated 5% of all cancers worldwide are thought to be related to alcohol intake."

Alcohol doesn't raise the risk of all cancers. But drinking is known to increase the chances of developing cancers of: mouth and throat, voice box (larynx), esophagus, colon and rectum, liver and breast (in women). Exactly how alcohol affects cancer risk is still being studied.



"The precise mechanisms linking cancer and alcohol aren't completely understood, but there are some hypotheses," Jain said. Among them:

- The body breaks alcohol down into a toxic chemical called acetaldehyde. Acetaldehyde is known to damage DNA, Jain said. Once DNA is damaged, a cell can start to grow out of control and form a cancerous tumor.
- Drinking alcohol increases blood levels of the hormone estrogen, which is linked to the risk of developing some types of breast cancer.
- Alcohol negatively affects how well the body can break down and absorb a variety of nutrients that may be associated with cancer risk, including carotenoids and vitamins A, C, D, and E.

Specific cancers may be tied to alcohol in unique ways. For example, people who drink tend to have lower amounts of folate in their diets, Jain said. That decrease has been linked to colon cancer.

Because of alcohol's ties with cancer, the American Institute for Cancer Research recommends not drinking at all. But according to the Dietary Guidelines for Americans, moderate alcohol consumption—for people who choose to drink—is OK. That means one drink a day for women or two drinks a day for men.

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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This virtual session will focus on popular nutrition myths and actual facts regarding nutrition and cancer. We will also discuss foods for optimal well-being for cancer patients during and after treatment.



Wednesday, November 18, 2020
12:00pm to 1:00pm

Register: <https://bit.ly/33Db8Lv>

For more information, call **215-214-1618** or email: RECstaff@fccc.edu



Fox Chase Cancer Center
Risk Assessment Program
Celebrating 29 Years
1991-2020

Editors: Yana Chertock, Lisa Bealin, Meredith Patrick, Joann Sicilia and Nicole Ventriglia

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