BRCA Women's College Cancer Genetics Newsletter

Issue 2: 2023

WOMEN'S COLLEGE HOSPITAL

WELCOME MESSAGE

We are excited to share our latest newsletter with you. Many of you reading this have participated in our various research studies and for that we thank you! It is because of your participation that we can answer several critical clinical questions for those at a high-risk of developing cancer.

In the last couple of years, we have strived to bring you the latest findings from our research team. We have done this with our newsletters, in addition to monthly virtual seminars. For those of you who were unable to attend the virtual seminars, these have been recorded and are available for you to watch on our Women's College Hospital Research Institute website. Again, it is your active research participation that allows us to generate very important research findings and we are thrilled to be able to share some of them with you.

As you are likely aware, one of our longest running studies at Women's College Hospital (WCH) is the Risk Factor Study. This is one of the largest studies of hereditary breast and ovarian cancer in the world. The data that we collect from you is helping to change practice and will improve outcomes for individuals who are at high-risk.

Notably, we want to inform you that we are actively transitioning to an online system that will allow us to collect questionnaire information in a more efficient and accurate manner. This online system, called REDCAP, allows participants and collaborating sites to update questionnaire information through a computer or other electronic devices. However, we will still have the questionnaires available via paper or .pdf fillable forms for those who prefer to participate this way.

We are fortunate to have many clinical, research and philanthropic partners. In this current newsletter, we are showcasing some of these important partnerships that enable us to continue this important work. We hope you enjoy the stories and research findings within this issue and please feel free to share with others who may benefit.

Finally, we thank you for your ongoing participation in our research program and we look forward to continuing our work with you.

Sincerely,
Steven A. Narod, MD
Kelly Metcalfe, RN, PhD
Joanne Kotsopoulos, PhD
Mohammad Akbari, PhD

RISK FACTOR STUDY NUMBERS

To date, there are over 18,571 BRCA1 and BRCA2 mutation carriers enrolled in our longitudinal study of high-risk women. We are extremely grateful to all our participants and their families. The information gathered in this study is critical for us to continue conducting research to improve upon prevention and management options. If you are not currently participating, please use this link to participate.

BREAST CANCER RISK AFTER 60

Breast cancer risk after age 60 among BRCA1 and BRCA2 mutation carriers
Stjepanovic N, Lubinski J, Moller P, Randall Armel S, Foulkes WD, Tung N, Neuhausen SL, Kotsopoulos J, Sun P, Sun S,Eisen A, Narod SA; Hereditary Breast Cancer Clinical Study Group.Breast Cancer Res Treat. 2021 Jun;187(2):515-523. doi: 10.1007/s10549-020-06072-9. Epub 2021 Jan 10.

For women over the age of 60 years with a BRCA1 or BRCA2 mutation, it was unclear if the risk of breast cancer was high enough to justify intensive screening. In this study, we evaluated breast cancer risk from age 60 to 80 years in women with a BRCA1 or BRCA2 mutation and no previous diagnosis of breast cancer or any previous breast prevention surgery. Over an average of eight years of follow-up, 61 invasive and 20 in-situ breast cancers were diagnosed in the group of 699 eligible women. The average risk of breast cancer per year was 1.8% for BRCA1 mutation carriers and 1.7% for BRCA2 mutation carriers. The cumulative risk of invasive breast cancer from age 60 to 80 was 20.1% for women with a BRCA1 mutation and was 17.3% for women with a BRCA2 mutation. Hormone replacement therapy, family history and oophorectomy were not associated with breast cancer risk. Findings from this large study indicated that the risk of developing breast cancer remains high after age 60 in both BRCA1 and BRCA2 mutation carriers. These findings suggest that there is a role for breast screening in older women with a BRCA1 or BRCA2 mutation.

OUTCOMES AFTER LAPAROSCOPIC OOPHORECTOMY

Patient reported experiences following laparoscopic prophylactic bilateral salpingo-oophorectomy or salpingectomy in an ambulatory care hospital.

Trister R, Jacobson M, Nguyen P, Sobel M, Allen L, Narod SA, Kotsopoulos J.Fam Cancer. 2021 Apr;20(2):103-110. doi: 10.1007/s10689-020-00208-y. Epub 2020 Sep 23.PMID: 32964297

At WCH, risk-reducing bilateral salpingo-oophorectomy is performed laparoscopically. As an ambulatory surgery, this means women can be released to go home within 24 hours after surgery unless there are serious complications. The objective of this study was to examine whether women undergoing prophylactic laparoscopic oophorectomy felt they were adequately informed about post-operative outcomes.

A telephone interview was conducted among 46 women undergoing surgery at the Familial Ovarian Cancer Clinic (FOCC) at WCH to collect detailed information regarding surgical outcomes, complications, symptoms, and time to return to daily activities. Most (78%) of the women felt well enough to go home. None of the women required a readmission to hospital. Forty-five percent of the women did not feel well informed about what to expect after surgery. Most of the patient-reported outcomes were expected and patient-reported menopausal symptoms were more common among women who were pre-menopausal and included pain and vaginal bleeding. In terms of returning to regular activities, pre-menopausal women resumed sexual activity later than post-menopausal women. On average, women returned to full-time work in 16 days. Despite patients receiving pre-surgery counselling, our findings suggest that there is a need to provide supplemental patient materials in preparing patients for what to expect after surgery. Using this information, we have developed an informational brochure along with a video to better educate women as they are preparing for preventive surgery.

FACTORS INFLUENCING MEMORY AND ATTENTION IN BRCA MUTATION CARRIERS

Kotsopoulos J, Kim SJ, Armel S, Bordeleau L, Foulkes WD, McKinnon W, Panchal S, Cohen SA, Sun S, Sun P, McKetton L, Troyer AK, Narod SA. An evaluation of memory and attention in BRCA mutation carriers using an online cognitive assessment tool. Cancer. 2021 Jun 2. doi: 10.1002/cncr.33654. Online ahead of print. PMID: 34077552

Among women in the general population (i.e. - no BRCA mutation), several factors negatively affect cognitive functioning (memory and attention). These include early surgical menopause and cancer treatment with chemotherapy, radiation, and/or tamoxifen. Although cognitive function does decline with age, whether other factors influence memory and attention in BRCA mutation carriers was not known. In a recent study of 880 women with a BRCA mutation, we used an innovative, online cognitive assessment tool called the Cogniciti Brain Health Assessment (BHA), to assess memory or attention. We then evaluated if various factors impact upon various aspects of memory or attention in this high-risk group of women. Importantly, we observed no impact of preventive surgery (oophorectomy or mastectomy), cancer treatment or hormonal factors on cognitive impairment beyond what was expected for the age of the women. Although these findings are reassuring, additional studies are needed to evaluate cognitive function over time when memory deficits become more prevalent.

DIRECT-TO-CONSUMER GENETIC TESTING AT WOMEN'S COLLEGE HOSPITAL

The Screen Project: Guided Direct-To-Consumer Genetic Testing for Breast Cancer Susceptibility in Canada Cancers 2021 Apr 15;13(8):1894
Steven A Narod, Nicole Gojska, Ping Sun, Angelina Tryon, Joanne Kotsopoulos, Kelly Metcalfe, Mohammad R Akbari

There is limited information regarding the outcomes of direct-to-consumer genetic testing (no pre-test genetic counselling) for BRCA1 and BRCA2 mutations. We initiated The Screen Project in 2017 to offer BRCA1 and BRCA2 genetic screening to all Canadians over the age of 18 who wish to know their mutation status. Patients enrolled in the study from 2017 to 2019 and were followed for one year after receiving genetic test results. Study subjects registered online and were sent a saliva sample kit, the individuals spit in the tube, and sent it back to the laboratory. There were 1,269 tested individuals between March 2017 and January 2019. A total of 1,157 (93%) were women and 87 (7%) were men. Sixty-six percent had a first- or second-degree relative with breast or ovarian cancer. Of the 1,269 tested individuals, 30 (2.4%) had a mutation in BRCA1 or BRCA2 (20 women and 10 men). Seventy-five percent of the females identified with a BRCA1 or BRCA2 mutation elected for a bilateral mastectomy and/or salpingo-oophorectomy within one year of receiving a positive result. Genetic counselling was available at no cost to all participants but was requested by only 5% of the non-carriers. The study subjects expressed a high degree of satisfaction with the process. This study demonstrates that direct-to-consumer generic testing represents a feasible and acceptable manner to offer genetic testing to all Canadians irrespective of geographic location.

CONTRACEPTIVE USE AND THE RISK OF OVARIAN CANCER AMONG WOMEN WITH A BRCA1 OR BRCA2 MUTATION

Gynecologic Oncology 2022 Mar;164(3):514-521
Yue Yin Xia, Jacek Gronwald, Beth Karlan, Jan Lubinski, Jeanna M McCuaig, Jennifer Brooks, Pal Moller, Andrea Eisen, Sophie Sun, Leigha Senter, Louise Bordeleau, Susan L Neuhausen, Christian F Singer, Nadine Tung, William D Foulkes, Ping Sun, Steven A Narod, Joanne Kotsopoulos, Hereditary Ovarian Cancer Clinical Study Group

Oral contraceptives (birth control pill) provide protection against developing ovarian cancer among women with and without a BRCA mutation; however, the impact of other types of contraception, such as intrauterine devices, implants and injections is not clear. Thus, we recently evaluated the relationship between the specific type of contraceptive and the risk of developing ovarian cancer among 3,466 women with a BRCA mutation.Using detailed information on contraceptive use that was collected from the research questionnaire, we observed that use of any type of contraceptive was significantly associated with a 38% reduced risk of ovarian cancer. More specifically, oral contraceptives offered a 34% reduction in risk and contraceptive implants were associated with a 70% reduction in risk. There were too few women who used injections or intrauterine devices, and this will be a topic of a future study. These findings support a protective effect of oral contraceptives and implants on risk of ovarian cancer among women with BRCA mutations. Despite this protective effect, bilateral salpingo-oophorectomy (removal of both ovaries and fallopian tubes) remains the most effective way to prevent ovarian cancer and death in women with a BRCA mutation.

CLINICAL SHOWCASE – BREAST SURGERY

Dr. John Semple & Dr. David Lim

The Department of Surgery at Women's College Hospital has a long legacy in providing excellent, compassionate surgical care and advancing innovation in breast surgery. Our team consists of three breast surgical oncologists (Dr. David Lim, Dr. Jaime Escallon and Dr. Tulin Cil) and three plastic surgeons (Dr. John Semple, Dr. Mitchell Brown and Dr. Katie Armstrong). Dr. Lim is the current Medical Director of the Breast Centre (and is supported by the Chair in Surgical Breast Cancer Research at WCRI) and Dr. Semple is the current Head of the Plastic Surgery division.

Together, our team provides expert evaluation and surgical management of both benign breast diseases and breast cancer for women in the Greater Toronto Area. Our plastic surgeons offer breast reconstruction, cosmetic and aesthetic breast surgery and gender-affirming top surgery. In particular, our institution is a center of excellence for providing risk-reduction mastectomies and immediate reconstruction for gene carriers and women with a strong family history of breast cancer. In addition to providing clinical care and advancing breast cancer care through research, the Department of Surgery is active in teaching medical trainees. All surgeons are affiliated with the University of Toronto Temerty Faculty of Medicine and provide teaching at the M.D. undergraduate and residency (post-graduate) level. The Division of Plastic Surgery also offers a Clinical Fellowship Program in Breast Reconstruction and has hosted International Fellows from all over the world.

ASK A SCIENTIST Q&A: DR. KELLY METCALFE

Rapid Genetic Testing for BRCA1 and BRCA2 Mutations at the Time of Breast Cancer Diagnosis: An Observational Study

Metcalfe KA, Eisen A, Poll A, Candib A, McCready D, Cil T, Wright F, Lerner-Ellis J, McCuaig J, Graham T, Sun P, Akbari M, Narod SA. Ann Surg Oncol. 2021 Apr;28(4):2219-2226. doi: 10.1245/s10434-020-09160-8. Epub 2020 Sep 28.PMID: 32989658

Q: What is rapid genetic testing?

A: In this study, rapid genetic testing was genetic testing that was done at the time of breast cancer diagnosis, and test results were available within 10 days. This is faster than what is generally provided in clinical practice. As a result, women with breast cancer had genetic test results available prior to the start of treatments, which allowed women and their care teams to use genetic test results to make treatment decisions.

Q: How are results of rapid genetic testing used when making breast cancer treatment decisions?

A: We have previously evaluated the impact of various treatments on the risk of new cancers and death in women with breast cancer and a BRCA1 or BRCA2 mutation. We reported that bilateral mastectomy (removal of both breasts) reduced the risk of developing a new breast cancer in the opposite breast, and also reduced the risk of dying. In addition, we have also reported that bilateral salpingo-oophorectomy (removal of the fallopian tubes and ovaries) reduced the risk of dying of breast cancer. In this study, women knew before they had surgeryif they had a BRCA1 or BRCA2 mutation and were able to use this information to make surgical choices based on scientific evidence.

Q: Can you tell us a little bit about the study?

A: On the day a woman was told she had breast cancer, her surgeon referred her into the study. Our genetic counsellor immediately contacted the woman and offered her an appointment for counselling and testing. If a woman consented, she then came to WCH for counselling and testing. Results were available within 10 days, and the genetic counsellor called the woman to give her the results.

Q: What were the results of the study?

A: Over 1,000 women participated in this study and we found that women who had rapid genetic testing used the information to make treatment choices. More than 70% of women who were found to have a BRCA1 or BRCA2 mutation elected for a bilateral mastectomy, compared to less than 20% of women who were found to have a negative result. Rapid genetic testing at the time of breast cancer diagnosis did not lead to elevated levels of distress, anxiety or depression. Overall, the great majority of women reported being satisfied with the process and would recommend rapid genetic testing to other women in their situations.

Q: What's next?

A: We are very excited to build upon the results of this previous study and recognize the need to increase access to rapid genetic testing for women at the time of breast cancer diagnosis. As a result, we are now leading a study where women from across Canada can access rapid genetic testing. For women who are diagnosed with breast cancer, a health care provider can refer a woman into the study. She never has to leave home to participate in this study. We courier a saliva kit directly to her house, she spits in the tube and ships the sample to the lab. Our study genetic counsellor receives the results within one week and calls the woman with her results. Women from across Canada are participating in this study, many of whom would not have had access to rapid testing where they live. We are evaluating this new way of delivering genetic testing and counselling to determine if outcomes are similar to what we observe with our traditional model of genetic counselling and testing. We have already enrolled around 500 women in this study and plan to test an additional 500 women. This video highlights how this study came about and why it is so important that more women have access to genetic testing at the time of diagnosis.

For more information on how to enroll in the study, please click here.

We are very grateful to patients like Stacy, who participated in this study. She shared her story in this video.

PHILANTHROPIC SUPPORTER SPOTLIGHT

In 2021, a donation from Women's College Hospital Foundation came through to the Familial Cancers Unit at WCH from Colleen Moorehead, business leader, author, philanthropist and change agent. The $100,000 gift provided important seed funding for a pivotal genetics research study at WCH that has the potential to do for breast cancer what the Pap smear has done for cervical cancer. One thousand women, including their relatives, are to be enrolled in a study, which uses a simple saliva test to determine BRCA gene mutation carriers. The outcome of this study has the potential to reduce cancer mortality rates among study participants by 70% and will be able to establish a new standard of cancer education, prevention, and care on a global scale to directly impact the survivorship rates of not only women, but families too. We sat down with Colleen to learn more about her and her inspiration for giving.

1.Tell us a little bit about yourself.

I am Chief Marketing Officer at Osler, Hoskin and Harcourt, a leading Canadian business law firm in Toronto. I am also a very proud donor and advocate for Women's College Hospital, having served on the Foundation's board of directors and been a volunteer leader for over 10 years. I am passionate about gender equity - in the workplace and in women's health. For too long, healthcare has not included a sex and gender lens when looking at research and disease, and we need to change that. There has also not been enough funding, at a systemic level, allocated to women's unique health research needs, I am on a mission to change that. Our health needs are different, and our health care solutions need to be different. We need protocols and system changes that identify women's health issues and provide solutions based on science – research as it relates to our bodies, whether that is our heart attacks, biological cycles, our mental health, or our cancers. We also need to support women from marginalized communities who are too often unfairly impacted by intersecting social determinants of health that affect health outcomes.

2.What inspired you to support the research that is being led by the Familial Cancer Unit at Women's College Hospital?

My biggest inspiration came from personal loss – I had a young niece who passed away from breast cancer in her early 30s. I think of her all the time. Her experience, and our experience as a family, led me to understand how an identified research protocol could have improved her health outcome and could have supported better health outcomes for other family members. Decision-making processes for treatment and care, based on science, always lead to better outcomes. The research that is being led by the Familial Cancer Unit at WCH is ground-breaking, just like the Pap smear protocol, which in 1947 was developed and implemented for detecting early symptoms of cancer.

3.Why do you continue to stay involved in helping us reach our goals of helping as many women with breast cancer as possible?

The research you are doing will absolutely create a seismic shift in how breast cancers, especially hereditary cancers, can and should be treated. When you look at how many women were saved because of the introduction of the Pap test, you know the same thing can happen with the introduction of the saliva test for the genetic screening of breast cancers. For me, knowing that if we support this research so that the team can have the data needed to inform treatment protocols for future generations, we will change outcomes. It is a dead-easy investment to make. When we fund this research creating a standard protocol to screen for genetic cancers in every hospital around the world, then we'd be able to catch more people at risk of developing cancer and save more lives. We just need to fund and complete the work.

4.What would you like to share about the importance of others getting involved in supporting a cause that they are passionate about?

Each of us can make a difference. If we don't support something we believe in, then nothing changes. Each of us can be the catalyst for change. With respect to the work being done by Dr. Metcalfe's team, I know she needs to enroll 1,000 people for her study, which costs money. If I can help her reach that number, by supporting her financially and using my voice to amplify the research to attract investment and patients, then I know the impact of that can mean lives saved. That's my motivation. We can't be bystander, that doesn't change outcomes. Being an active supporter allows us to become a part of something bigger than we are. It allows us to change the world for women and their families.

The study being conducted by the Familial Cancer Unit at Women's College Hospital will cost $1 million to reach the required 1,000 enrollees and provide the screening kits. If you would like to donate, please visit www.wchf.ca

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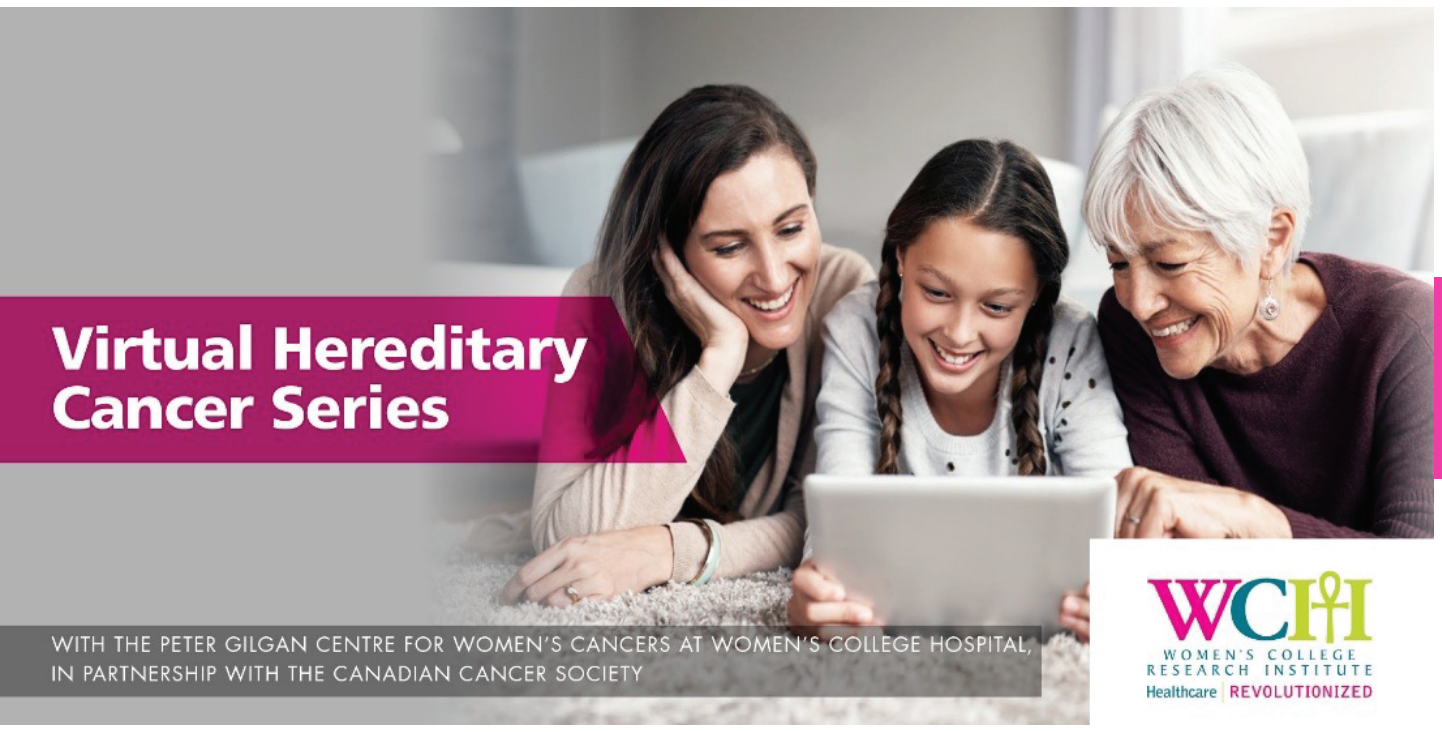

VIRTUAL HEREDITARY CANCER SERIES

Click here to connect with and learn from leaders in hereditary breast and ovarian cancer research and treatment.

The Risk Factor Study is funded by the Canadian Institutes of Health Research and The Peter Gilgan Centre for Women's Cancers at Women's College Hospital, in partnership with the Canadian Cancer Society.

THE PETER GILGAN CENTRE FOR WOMEN'S CANCERS

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

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