CONSENT FORM for POPULATION BASED BRCA GENETIC TESTING IN CANADA

PRINCIPAL INVESTIGATORS: Dr. Steven Narod
Dr. Mohammad Akbari

SITE: Women's College Research Institute
Invitae

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Our research group at Women's College Hospital would like to invite you to take part in a new research study of genetic testing for BRCA1 and BRCA2 in Canadian men and women. This study is called 'Population based screening for BRCA genetic testing in Canada". The study team includes, Dr. Steven Narod, Dr. Mohammad Akbari, Dr. Kelly Metcalfe and Dr. Joanne Kotsopoulos. Angelina Tryon is the study genetic counsellor.

Please read this consent form carefully. You may have this form and all information concerning the study explained to you. You may take as much time as you wish to decide whether or not to participate. Feel free to discuss it with your friends and family, or your family doctor. If you have any questions, please contact Angelina Tryon, Genetic Counsellor at 416-323-6400 ext. 2727 or Dr. Steven Narod at 416-351-3765.

BACKGROUND

Breast cancer is the most common cancer among Canadian women and affects approximately 1 in 9 women. In men, prostate cancer is the most common cancer, affecting about 1 in 8 men in their lifetime. The majority of these cancers (>90%) happen for reasons we do not fully understand. However, approximately 5-10% of all cancers are hereditary and due to a mutation (or change that causes the gene to not work properly) in a gene that is passed down from one generation to the next. Two such genes, include BRCA1 and BRCA2. About 1 in 200 Canadians have a mutation in BRCA1 or BRCA2. Women with a BRCA mutation have a high lifetime risk of developing breast and ovarian cancer. Men with a BRCA mutation are at increased risk of developing prostate and other cancers. Several options are available to detect cancers early or reduce the risk of cancer from happening. For women, these options can include intensified screening, taking medications to reduce cancer risks or preventative surgery. For male BRCA carriers, options can include additional prostate screening (using both the PSA blood test and a digital rectal exam) starting at a younger age.

More information about the BRCA1 and BRCA2 genes tested in the study is included on the study website (www.thescreenproject.ca). Please review this information to learn more about the genes being tested, the possible types of results, and the implications of testing for you and your family before deciding if you want to participate in this research study.

Currently, genetic testing for BRCA1 and BRCA2 is offered to eligible women and men by provincial programs, such as the Ontario Ministry of Health and Long Term Care or British Columbia Ministry of Health. For individuals interested in genetic testing, there are eligibility criteria that must be met in order to qualify for testing, including age at cancer diagnosis, ethnicity, and family history of breast or ovarian cancer. Therefore, BRCA testing in Canada is only available to selected individuals with a strong personal or family history of cancer. As standard practice, an eligible patient is currently provided in-person genetic counseling at a local genetics clinic prior to BRCA testing. Wait-times for clinic appointments vary, but may be up to 6 months to one year. The average time to receive test results after giving a blood (or saliva) sample is 6 – 8 weeks in Ontario; however, this varies based on province and can take up to 8 – 10 months.

To date, patients who are not eligible have limited options to pay out of pocket for genetic tests, available through out of country laboratories; however, the cost of testing ranges from $700 - $1500 USD. Much of this testing is provided using a direct to consumer (DTC) approach. This approach to genetic testing means that testing is initiated directly by the patient, rather than through a healthcare provider like a genetic counsellor, and may or may not require a physician to order the genetic test.

We wish to make genetic testing for BRCA1 and BRCA2 accessible to all Canadians at an affordable price, $299 USD. Through widespread testing, we aim to identify men and women with a genetic predisposition to developing cancer using a guided DTC genetic testing approach. We wish to bring DTC genetic testing for BRCA1 and BRCA2 to all Canadians that is guided by medical professionals with ongoing, long-term follow-up and management options,

particularly for individuals identified with a BRCA1 or BRCA2 mutation.

PURPOSE OF RESEARCH STUDY

The purpose of this research project is to establish a population based model for BRCA genetic testing in Canada. You are being asked to participate because you are over the age of 18 and are currently living in Canada. We hope that through this population based approach, we can identify BRCA mutation carriers in Canada before they develop cancer so that they can be offered preventive, risk-reducing options. We also aim to measure the levels of satisfaction and cancer-related worry (level of worry and feelings both before and after genetic testing) associated with a population based, guided direct to consumer approach to BRCA genetic testing. It is hoped that our research may lead to accessible genetic testing for hereditary cancers in Canada.

WHO IS ELIGIBLE TO PARTICIPATE?

- Women and men who are living in Canada (ie. have a Canadian mailing address)
- Women and men who are 18 years of age and above

Individuals who are not currently eligible for a provincially-covered test, as well as to those who may qualify but experience some barriers to accessing genetic counselling and testing through their province or local genetics program are eligible for the study. If you are interested in BRCA genetic testing, you may also wish to speak with your doctor or local genetic counsellor to determine if you are eligible to receive this genetic test (at no cost) based on your provincial criteria.

It is anticipated that 10, 000 women and men across Canada will participate in this study. The length of this study for participants is 1 year. The entire study is expected to take 3 years or will be completed when we enrol 10, 000 participants.

WHAT WILL HAPPEN DURING THIS STUDY?

If you are eligible and choose to participate in this study, you give permission for the study team to collect the following information:

- Demographic information
- Personal and family history of cancer
- Level of worry about developing cancer

You will have access to additional educational information on the study website prior to deciding to participate and consenting into this study.

In order to offer BRCA1 and BRCA2 genetic testing through this study we have partnered with Invitae. Invitae is a genetic testing company in the United States offering genetic testing for many genes. Invitae runs a CLIA-certified laboratory (testing facilities that meet the standards and hold certificates for clinical laboratory testing on humans as set out by the Clinical Laboratory Improvement Amendments (CLIA) program).

If you chose to participate, you will provide consent. At this time, your genetic testing is ordered within 5 business days by the study team using Invitae's online requisition form. Your name, date of birth, sex, ethnic background, address and email address will be provided to Invitae on the test requisition form. This information is required for sample identification, shipment of your genetic testing kit and generation of your genetic test results report.

Invitae will perform genetic testing and interpretation for all study participants for the price of $299 USD. Invitae will contact you directly using the email you provide, to collect your payment information. Therefore, if you participate, you will provide consent, receive a saliva (spit) collection kit and pay $299 USD out of pocket to Invitae to receive your BRCA genetic test results. The study team at Women's College Hospital will not profit or receive funds from Invitae. Invitae will ship a saliva (spit) collection kit to you. Genetic testing will be done at Invitae using this saliva sample. No genetic test results will be released until you have paid $299 USD to Invitae. Women's College Hospital does not guarantee the accuracy of the genetic testing performed by Invitae. Any diagnostic genetic laboratory may produce false positive or false negative results due to a variety of reasons. Your genetic test results will be available within approximately 2 to 4 weeks from the time your saliva sample is received by Invitae. Any samples sent to Invitae become eligible for destruction 60 days after a result has been released or upon cancellation

of the test. No DNA will be transferred or held at Women's College Hospital for the purpose of BRCA genetic testing during the study period.

Test Results:
A copy of your genetic test results will be sent to our study team at Women's College Hospital by Invitae through the Invitae online portal. This study will report either: 1) *negative*, meaning no known cancer-predisposing mutations were found based on our current knowledge or 2) *positive*, meaning a mutation (pathogenic or likely pathogenic variant) with a known clinical impact was found or 3) *variant of uncertain significance*, meaning a genetic change (or variant) was found in BRCA that is not conclusively shown to cause cancer and the significance is currently unknown. Negative reports will be made available directly to participants through the Invitae portal without additional genetic counselling, unless requested by the participant after they receive their results. All positive and VUS reports will be made available to participants after initial results disclosure over the telephone by the study genetic counsellor.

Participants who receive a positive result will be notified the study genetic counsellor. Follow-up appointments will be offered, in person or by telephone, to discuss the implications of participants' results, to provide genetic counselling and to arrange appropriate referrals. If you prefer, you can be referred to a local genetics clinic in your area.

If your results are negative, this does not mean you will not develop cancer. If you have a family history and would like more information about additional genetic testing, you may wish to speak with a genetic counsellor at your local genetics clinic. A negative (uninformative) result can sometimes be frustrating and can increase worry, or it can provide relief. Follow-up genetic counselling by the study genetic counsellor will be available upon request.

If you receive an inconclusive or variant of uncertain significance result, you will be notified by the study genetic counsellor. The genetic counsellor will be available to provide counselling and additional information. Our knowledge of genetics is evolving and we may know more in future about particular genetic variants. You may also wish speak with your primary healthcare provider and be referred to a local genetics clinic for long-term follow-up.

Only the BRCA1 and BRCA2 genes are included in the initial genetic test, as part of the study. Other genes related to cancer predisposition will not be tested automatically. However, please see the 'Optional Genetic Testing' section of this consent form for information on how you can request additional genetic testing related to hereditary cancers. If you wish to learn about other medical or genetic conditions, please speak with your family doctor or local genetic counsellor.

Follow-up:
In addition to the information you provide prior to participating and genetic testing, you will be asked to complete two follow-up questionnaires upon receiving your genetic test results. The first is a short questionnaire to assess your satisfaction with the Screen Project and you will have the opportunity to provide feedback based on your experience. The second is dependent on your results. One year after you receive your BRCA genetic test results, you will be asked to complete a brief follow-up questionnaire if you receive a positive BRCA test result. If you receive a negative or inconclusive result, you will be randomly (like flipping a coin) selected to complete the follow-up questionnaire. This questionnaire will be available online and is meant to evaluate your level of satisfaction, health and risk-reducing strategies and your level of worry related to developing cancer following participation in this study. In addition, if you provide additional consent (on page 6), the study team may communicate with you in the future regarding your interest in new or follow-up research studies.

Optional Genetic Testing:
In addition to genetic testing for mutations in the BRCA1 and BRCA2 genes, you may give study researchers permission to request additional genetic testing analysis for other hereditary cancer genes on your saliva sample. Additional genetic testing analysis would be completed by Invitae using data from the testing of the original sample you provide for the study, and you would not need to provide an additional sample. This additional testing is free if it is requested within 90 days of the date you provide your saliva sample. Any additional testing beyond the BRCA1 and BRCA2 genes is not done automatically. If you opt to have this additional genetic testing, you must contact the study team by email at thescreenproject@wchospital.ca. As stated above, this request must be completed within 90 days of the date you provide your original saliva sample. The results from the additional

analysis would be available approximately 10-21 days after this extra testing is requested. The results of the additional analysis will be available on the Invitae portal after you submit your request for that to the study team and you can access it through your account on the Invitae portal. It is recommended to contact Invitae for requesting an appointment for a phone-based genetic counseling session with one of the company's genetic counselors or follow up with a local genetic counselor or medical professional with respect to the additional testing report.

Results from this additional genetic testing will be linked to the data collected as part of this research study and may be used for research purposes. Giving study researchers permission to request additional genetic testing analysis on your sample is optional and you may indicate your preference on the consent page. Please note that simply indicating your preference on the consent form regarding additional testing does not automatically request this testing. You must contact the study team by email at thescreenproject@wchospital.ca within 90 days of the date you provide your original saliva sample to complete the request.

BENEFITS

You may or may not benefit from participating in this study. It is anticipated that information collected from this study will help provide all Canadians with access to genetic testing for hereditary breast and ovarian cancer. Genetic test results from this study may also allow you to better manage your health and understand your risks for developing specific types of cancers.

RISKS

There are no known risks associated with the collection of saliva. In addition to any unforeseeable risks in this study, potential risks of this testing are primarily psychological in nature. An increased risk of cancer or uninformative test results can lead to psychological consequences including feelings of depression, regret and distress. If you receive a positive result, you may also be faced with making important decisions about cancer risk-reducing options and other aspects of your health. Please consider whether you feel emotionally ready to receive information about your BRCA mutation status and take time to consult with family, friends and other healthcare providers. If you require additional support, you may speak with the research team who can discuss additional support options available to you.

As of May 4, 2017, the Genetic Non-Discrimination Act (GNA), formerly known as Bill S-201 was passed into law in Canada. This law protects individuals from the use of genetic test results for means of discrimination by potential or existing insurers. Under GNA, insurance providers cannot request or require that a person undergo genetic testing or disclose previous and/or future genetic test results. However, GNA does not prohibit insurers from using information about pre-existing or previously diagnosed medical conditions. Family history is not protected by GNA. No information in regards to your genetic test results will be given by Women's College Hospital or members of the study team to your insurance company without your authorization, unless, in the unexpected and very unlikely event, Women's College Hospital or members of the study team are obliged by legal process to do so. You may contact the study team for additional information about GNA.

Please note that due to the rapid pace of technological advances, the potential future use of genetic information is unknown and therefore the potential future risks also are unknown.

CONFIDENTIALITY

Your medical history and study information will be kept strictly confidential. Your confidentiality will be respected to the extent permitted by applicable laws and regulations and your study records will not be publicly available. No information that discloses your identity will be released or published without your specific consent. Your identity will not be used in any reports or publications about the study; you will only be identified by a study number. All information collected from the baseline, genetic test results and follow-up questionnaires will be kept behind locked doors and in secure computer files and is subject to the confidentiality and privacy regulations of Women's College Hospital. This information will not become part of your medical record. If you participate, your information will be available only to the research team. Women's College Hospital will share only relevant demographic, as well as personal and family history information, collected at the time of consent with Invitae for the sole purposes of sample identification, shipment of your genetic testing kit and generation of your genetic testing report. The study team at Women's College Hospital will not share information collected on the initial study questionnaires with any other party. Information regarding your medical history or test results will not be disclosed to any family members,

insurance companies or healthcare provider without your consent. Please note that genetic information cannot be protected from disclosure by court order. Your samples will be sent to the US. Any study related data sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries dealing with protection of information may not be as strict as in Canada.

PARTICIPATION

Your participation in this study is voluntary. You may withdraw from the study at any time. You can choose not to participate or you may withdraw at any time by notifying the study team by telephone. If any new information becomes available that is relevant to your decision to continue to participate or withdraw, it will be provided to you or your legal representative by the study team as it becomes available. You will not have to provide a reason for withdrawal. If you withdraw your consent, information collected about you prior to your withdrawal will still be used. No new information will be collected and no testing will be performed without your permission. You may cancel the BRCA genetic testing performed on your sample at any time prior to the test being completed; however, Invitae cannot process a refund if you have paid for your test. If you withdraw from the study your saliva sample or leftover DNA sample will be discarded at your request.

In no way does signing this consent form waive your legal rights, nor does it relieve the study team or involved institutions from their legal and professional responsibilities. The study team may end the study at any time and for any reason.

ADDITIONAL USE & TRANSFER OF SAMPLE:

Any samples sent to Invitae become eligible for destruction 60 days after a result has been released or upon cancellation of the test. The Women's College Hospital study team will not be responsible for the additional use of your sample by Invitae.

Any DNA changes or variants identified through your BRCA genetic testing by Invitae may be shared in ClinVar or other HIPAA (Health Insurance Portability and Accountability Act) -compliant public databases by Invitae, intended to aid the medical community in the interpretation of genetic changes and conditions. In all cases, your sample information will be de-identified before any information is shared.

Invitae may use your genetic samples and personal information to create a data set that omits your name, home address, and other information that can directly identify you, except with the use of a key code that is held separately from the data set. This data set is called "pseudonymized data." Pseudonymized genetic data can significantly speed up medical research, which can help increase understanding of genetic conditions, improve genetic testing, find new treatments, and eventually prevent disease. Specifically, by signing this consent, you consent to the following uses of your pseudonymized data:

A. Pseudonymized genetic information: Invitae may keep, use, and/or share your pseudonymized genetic information for validation, research, quality, and/or educational purposes, except as prohibited by law.

B. Pseudonymized samples: Invitae may keep, use, and/or share your pseudonymized samples for validation, research, quality, and/or educational purposes, except as prohibited by law.

Your data and personal information will be stored and protected as required by law. Invitae will share the clinical report, which includes your personal information, with the following individuals and entities:

- The healthcare provider(s) listed on the test order form.
- Domestic and foreign regulatory agencies and government officials who have a duty to monitor or oversee genetic testing.

YOUR RIGHTS TO YOUR PERSONAL INFORMATION:

You have certain rights with regard to your personal information. You have the right to request access to, correction, or deletion of, your personal information. You also have the right to object to or restrict Invitae's use of your personal information. Finally, you have a right to request that Invitae move, copy, or transfer your

personal information to another organization. In order to make any such requests, you can submit your request via email to privacy@invitae.com.

You can log in to the Invitae patient portal (www.invitae.com/patients/signin) and click on Account Settings > Preferences to allow Invitae to contact you in the future regarding research opportunities.

You should know that your rights may be limited if Invitae is unable to identify you because, for example, your personal information has been anonymized or your name and other direct identifiers have been removed from your data set. You also should note that your rights have the following limitations:

- If your information has already been used or shared, it cannot be unshared or destroyed;
- your pseudonymized genetic information and/or sample(s) may still be used to develop new tests and to improve or confirm the quality of existing tests, including sharing pseudonymized data with public databases (such as ClinVar), except as prohibited by law; and
- Aggregate information that includes your genetic information (for example, summary information like the total number of patients tested with a particular variant), may still be shared with third parties for research or education purposes.

REQUEST FOR MORE INFORMATION

If you have any questions regarding participation in this study contact: Angelina Tryon, Genetic Counsellor at 416-323-6400 ext. 2727. If you have any questions about your rights as a research participant, please contact the Chair of Research Ethics Board at ethics@wchospital.ca. This person is not involved with the research project in any way and calling will not affect your participation in the study.

You can read Invitae's Privacy Policy and Notice of Privacy Practices (available at www.invitae.com/privacy). You may contact Invitae's Chief Privacy Officer/Data Protection Officer with questions about the use of your information and to exercise the rights you have in your data at privacy@invitae.com.

DOCUMENTATION OF IMPLIED INFORMED CONSENT

Study Title: POPULATION BASED BRCA GENETIC TESTING IN CANADA

Name of participant: _____

By completing the questions below, I confirm that:

☐ I have read each page of the consent form and have downloaded a copy;
☐ I have contacted the research team with any questions and they have been answered to my satisfaction;
☐ I understand the requirements of participating in this research study;
☐ I understand the potential risks and benefits of participating in this research study;
☐ I understand the alternatives to participating in this research study;
☐ I understand the rights of research participants;
☐ I have reviewed all the study materials available on the study website www.thescreenproject.ca;
☐ I understand that my participation is voluntary and that I may discontinue participation in the study at any time;
☐ I understand that this study evaluates the BRCA1 and BRCA2 genes and will not test for other genes related to breast and ovarian cancer, unless it has been requested after disclosing the initial result (find out more about additional testing at the bottom of this page);
☐ I understand that if I want more information about other genetic conditions or genetic tests, it is my responsibility to speak with a local genetic counsellor or health care provider;
☐ I understand that the ordering physician on this test is part of the research team for this study and is not my medical provider
☐ I authorize access to my personal health information and research study data as explained in this form;
☐ I understand that Invitae (https://www.invitae.com/) will perform the genetic testing and reporting of the results.

□ I acknowledge that Invitae handles and uses my data provided by the study team for performing my genetic test in accordance with Invitae's Notice of Privacy Practices and Privacy Policy located on its website (https://www.invitae.com/privacy/).
□ I authorize Invitae to release my BRCA genetic test results to the study team at Women's College Hospital;
□ I have agreed, or agree to allow the person I am responsible for, to participate in this research study

I give permission to the study team to contact me if additional information is needed in the future.

YES _____ NO _____

Contact Information: Telephone: _____ Email:_____

I give permission to the study team to contact me for future studies and follow-up outside of this study period.

YES _____ NO _____

Additional Genetic Testing:
I give permission to the clinical study team at Women's College Hospital to request additional genetic testing analysis on my saliva sample at Invitae for other cancer-causing genes (other than the BRCA1 and BRCA2 genes), which may be linked to data collected as part of this research study:

*this testing is available at no additional cost and can be ordered by the Screen Project clinical team within 90 days of your BRCA1 and BRCA2 genetic testing order
YES _____ NO _____

DISCLAIMER: Participants who would like additional genetic testing for hereditary cancers must contact the study team at Women's College Hospital at thescreenproject@wchospital.ca within 90 days of providing their sample to acknowledge their consent and interest to proceed with additional genetic testing. By selecting "YES" on the above question, the clinical study team will NOT automatically order additional genetic testing on your saliva sample at Invitae, without receipt of participants' written email confirmation of interest and consent for additional genetic testing by the study team.

Please check the appropriate box:

☐ I **consent** to participate in this study. By checking this box, you are indicating that you have read and understood this consent form and that you agree to participate in this study.