

Supplemental material

APPENDIX 1: Patient/guardian information sheet

Parent/Guardian Information Sheet

(For Parent/Guardian providing consent for the participant)

Introduction

Your child is being invited to take part in the PREDICT study because they have been diagnosed with cancer. The PREDICT study aims to understand the genetic cause of cancer affecting children and young people who are 21 years old or younger.

This Parent/Guardian Information Sheet and Consent Form tells you about this research study. It explains the tests and research involved. Knowing what is involved will help you decide if you want your child to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not your child can take part, you may wish to discuss this with your child, a relative or friend, and your child's doctor.

If you decide you want your child to take part in the PREDICT study, you will be asked to sign the consent section. By signing consent you are telling us that you:

- Understand what you have read
- Consent to your child taking part in the PREDICT study
- Consent to your child undertaking tests, which are outlined in this information sheet for the purpose of this study
- Consent to the use of your child's personal and health information as described.

You will be given a copy of this Parent/Guardian Information and Consent Form to keep.

Your child's participation is voluntary

Your decision to have your child participate in this study is completely voluntary and there will be no cost to you. If you do not want your child to take part in this study you do not have to. You should feel under no obligation to have your child participate in this study. Choosing for your child not to take part in this study will not affect your child's current and future medical care in any way. Whatever your decision, please be assured that it will not affect your child's medical treatment or your relationship with the staff who are caring for your child.

Your child's withdrawal from the study

You are under no obligation to have your child continue with the research study. You may change your mind at any time about your child's participation in the research. People withdraw from studies for various reasons and you do not need to provide a reason. You can withdraw your child from the study at any time by completing and signing the "Withdrawal Form" included with this Information Sheet.

If you withdraw your child from the study, you will be able to choose whether the study will destroy or retain the information it has collected about your child. You should only choose one of these options. Where both boxes are ticked in error or neither box is ticked, the study will destroy all information it has collected about your child.

If you withdraw your child from the study, information collected about your child that has already been analysed and/or included in a publication may not be able to be withdrawn or destroyed. In such circumstances, your child's personal information will continue to form part of the study's records and results. Your child's privacy will continue to be protected at all times

What is the purpose of this research?

Genes are what make up DNA – the chemical structure carrying your genetic information that determines many human characteristics such as the colour of your eyes or hair.

Researchers study genes to understand why some people have a certain condition, like cancer, and why some people do not. Understanding why cancer occurs in some people may help explain why some people respond to a treatment, while others do not, or why some people experience a side effect and others do not.

This study is focused on **Cancer Predisposition Syndromes (CPS)**, which are linked to an increased risk of developing certain types of cancer. Changes in a gene which affected their function are called 'gene faults' or 'mutations' and if the fault is in a cancer predisposition gene, this change can be linked to a CPS.

The PREDICT study will collect a blood sample and test the DNA of newly diagnosed cancer patients to look for CPS. If we find that your child has a CPS, it may mean they have an increased chance of other cancers. It may tell your child's doctor:

- If there are ways to check for cancers early
- How to help stop cancer happening
- About treatments that may help and which ones might not help

The purpose of this study is to:

- Show that this type of genetic test is useful and will accurately benefit patients at increased risk of cancer
- Improve the outcome for children with cancer and their families

Was my child's CPS inherited?

CPS can be passed down to a child from one or both of their parents (inherited) or may not be inherited at all and occur in a child for the first time when they are born.

If you agree for your child to join the study, we will also ask you, as his/her parent(s) to provide a blood sample. We will use your sample as a comparison tool in the analysis process of your child's sample. We will collect your DNA from the blood sample. If after two weeks your blood has not been collected, you will receive a reminder email. We recommend that you have your blood collected within 4 weeks of consenting.

If we find a CPS in your child, then we would test your DNA for the **same** gene fault found in your child. However, we only look for faults in parents' DNA if their child has been found to have a CPS.

If we find the same gene fault in one or both of you, you may also have a CPS. If you have CPS, it means:

- Your child has inherited the CPS from you
- You may have an increased chance of cancer
- Your blood relatives (sisters, brothers, nieces, nephews) may also have a CPS. If they want to find this out, they will be offered a referral to a specialist.
- It may also help you (as parents) to see if there are ways to avoid cancer in any future children.

What does participation in this research study involve?

Let us collect your child's health information from their hospital medical record

This information will include general information about your child (such as date of birth, sex, hospital) and details of their cancer (such as test reports and treatment).

Let us collect information about your child's relatives

This information will include details of any relatives who have had cancer or health problems at birth. To collect this information, you will be asked to fill out a web-based (or paper-based if you prefer) questionnaire for each family member. You may receive a call from the study genetic counsellor to clarify or expand some of your family history.

You may have previously provided your family history of cancer during attendance at the Family Cancer Clinic. To avoid repetition for you, we will access your clinic file and collect family history for use in this study.

Let us collect your child's DNA

We will need to get a sample of your child's healthy (non-cancer) cells from which to collect their DNA. These healthy cells can be taken from about 5ml (about 1 teaspoon) of blood. Where possible, the blood sample required for this study will be taken at a time when blood is taken as part of routine medical care so no extra needle puncture would be required. Blood can either be taken from a vein in the arm or from a central line if your child has one. In some situations normal (non-cancer) cells will need to come from a skin biopsy.

Let us test your child's DNA for faults in genes linked to cancer to look for a CPS

The study test looks for change in your child's genes but only those genes known to be linked to CPS. The detected changes will first be checked by a panel of specialists who will review if these changes are relevant or not. The relevant changes will be given to you by your child's doctor.

Where possible, we would also like to test DNA from both parents. This is to help us understand the findings in your child. If we find a gene fault in your child, this will also help us to see if one or both parents have the same gene fault. If one or both of you have the same gene fault as your child, then this may suggest that your child's CPS is inherited.

Help us understand your family's experience with being part of this study

To do this, we have developed some brief surveys that will be given to you throughout the study:

- I. At study enrolment, after you receive your child's results from the study (if you choose to), and then every year for three years. These will take about 15-20 minutes.
- II. We will also send you some other very brief surveys, every 3 months. These will only take about 2-5 minutes.

Our surveys will ask you:

- How your child is feeling physically (e.g., whether they are feeling well and have enough energy);
- How your child is feeling emotionally (e.g., whether they are feeling happy or stressed);
- What your child thinks of the study and about taking part (e.g., their satisfaction, any regrets); and
- If we can do anything to improve the study for future families.

Your child can participate in these surveys even if you do not wish to, and vice versa. We also understand that you may not wish to do all or some of these surveys. So, we will contact you before each survey is sent to see if you want to complete it. If you don't want to be contacted about completing surveys, we will send you a form to withdraw from this part of the study. Your child can still participate in the other parts of the study. Whatever you decide your decision will not affect your child's care in any way.

Let us follow up with your child's doctor after the testing has been done

If we find your child has a CPS, we will collect the following information for a period of up to 5 years:

- How your child's doctor used the genetic results in their treatment

- If your child's doctor referred you and your child to a Genetics Service to talk about the research results. If not, we would like to understand the reason.
- As part of this study, we will also collect information from the Genetics Services.

If we do not find a CPS in your child, we will still collect clinical information (e.g., treatment information) to understand the implications of these findings.

What might the genetic test result say?

I. We did not find that your child has a gene fault linked to CPS

This is the most likely result. However, your child may still have a CPS gene fault that we were not able to find with the current knowledge.

II. We found your child has a gene fault known to be linked to a CPS

Your child's doctor will talk to you about whether knowing this result can help their treatment. You and your child may be referred to a group of specialists who works at a Genetics Service.

III. We found a fault in one of your child's genes that we looked at but we do not know if it is linked to a CPS

We need to do more research. So, we won't usually tell your child's doctor about this result.

Do we have to get the results of my child's genetic testing?

When the results are ready, you and your child can talk to your child's doctor about what the test found. Even if a CPS is found, you may choose not to know. During the study, at any time, you can also tell us not to re-contact you to receive the result. We will still check with you when the results are available just in case you have changed your mind.

Are there possible benefits from being part of the study?

If your child is found to have a CPS, it may mean they have an increased chance of getting another cancer in the future. So, your child's participation in this study may allow them to undergo some additional screening, which can assist in the early detection of another cancer in them.

If your child has inherited a CPS, this study might also:

- Help you (as parents) and your blood relatives find out if you have a CPS.
- Be helpful to others in the future with the same cancer as your child.
- Help to make tests to find cancer and find new forms of treatment.
- Tell us how we can work with you and families like yours when we do genetic testing.

By testing your DNA it may also help to find out more about the genetic cause of cancer.

Are there possible risks from being part of the study?

Blood collection

Any complications with getting a blood sample from your child or you for this study will be small. Where possible, the sample will be taken from your child at a time when blood is taken as part of their routine medical care. If a central line is in place, we will draw blood samples from the line.

When getting the blood sample there can be:

- Slight pain where the needle is put in and/or some minor bruising, which may last one to two days.
- A small chance of bleeding or infection.

These complications would also apply to you when giving a blood sample.

Genetic testing

If your child (or you) is found to have a CPS, it may be upsetting and the findings may affect family relationships. Genetic counsellors working in the Genetics Service will be there to support you and your family. On the other hand, some families experience relief from knowing what is behind the cancer that has happened to your child.

It is possible that the study may not find any gene fault related to your child's cancer diagnosis. Some people may find not getting an answer upsetting.

If your child has a CPS, we look at both your child's and your genes (where possible). In doing this, there is a small chance that the test could identify family relationships that are different from expected. We will not report these findings.

Incidental findings

There is a small chance, thought to be less than 10%, that the study test may identify a genetic change (also called a mutation) in your child's normal cells which might be associated with an increased risk of developing other health problems.

Sometimes these health problems might be important for your child's future care and for your family. This is called an incidental finding. If an incidental genetic change is found in your child's normal cells, the finding will be reviewed by an appropriate panel of specialist doctors including laboratory and clinical geneticists.

The specialist review will determine whether the genetic change is known to be significant for your child's health. If so, this will be reported back to your child's doctor. It will also be recommended that your child and your family be referred to a Genetics Service for counselling and a specific management plan, and, if appropriate, to confirm this research finding in an accredited laboratory.

What will happen to my and my child's blood and DNA samples?

During the study, samples will be stored at the Children's Cancer Institute in Sydney. Personal details linked to the samples are stored separately. At any time, you can withdraw your child or yourself from this study or request the samples be destroyed. This can be done by completing the "Withdrawal Form" included with this Information Sheet.

Genomic analysis will be carried out on a validated industry-standard pipeline that is compliant with all privacy and security regulations. Blood and/or DNA samples may be sent for related testing to other laboratories. These may be in Australia or overseas. Before sending, any linked personal details will be removed.

You can choose to let us store any of your child's samples and your samples (if collected) left over after the testing has finished for this study. The samples would be stored for at least 15 years from when the study publishes its final report at the Children's Cancer Institute for future research studies.

All proposals for future research on the stored samples will be reviewed for scientific merit. They must also have approval from a Human Research Ethics Committee. Researchers who use your child's samples in these research studies may need to have information about your child's cancer, such as treatment response and outcome. However, this information will be shared in a de-identified manner to protect their privacy.

What will happen to my child's personal and health information?

By signing the consent, you agree to allow study investigators and relevant clinical and laboratory research staff involved in the study to collect and access your child's personal and health information. Your child's personal and health information will be accessed, used and stored in accordance with Australian privacy laws. Additionally, any personal and health information we obtain from you for the purposes of this study will be managed in the same way.

Any information obtained in connection with this research study that can identify your child will remain confidential. Access to this information will be strictly restricted to researchers involved in the PREDICT research study at the Children's Cancer Institute, the Sydney Children's Hospital, the Children's Hospital at Westmead and their delegates under which the research study is conducted.

Information about your child which is specifically related to the study will be collected using the RedCap database, hosted by UNSW. All information will be stored and backed up on their server, which is located within Australian borders, in the form of a computer file. Research report forms will be kept in paper hard copies and archived to a secondary storage facility on completion of the study. After the completion of the study, all study participant information will be kept in a secure secondary storage facility.

Within a period of up to 15 years of the publication of the study's final report, all soft copies of study participant information will be destroyed. Additionally, all hard copies will be

shredded and destroyed by a secured destruction service provider. However, non-identifiable data will be stored indefinitely, with the possibility that this data may be used for future related or unrelated studies.

Clinical information and genetic data from both your child's DNA and your DNA (if tested) will contribute to research databases or registries either in Australia or overseas. This allows researchers from all over the world to share data and accelerate cancer research. This can be a public database where the public can access limited de-identified information such as cancer type, age group and gender, and specific changes in the genes. It can also be a controlled database where doctors and scientists will apply for access to more detailed but de-identified clinical and genetic information for the purpose of answering specific research questions, which may or may not be related to this study.

It is anticipated that the results of this research study will be published and/or presented in a variety of forums. However, identifiable information (e.g. name, date of birth, photographs) will *not be* included, except with your permission that is separate to this consent. Given the nature of the medical information that may be included, it *may* be identifiable to you, some healthcare providers involved in your child's care, and possibly close relatives.

Measures used to secure this information have been approved by the Human Research Ethics Committee. Information gathered for the study will only be used for the purpose of this research study and it will only be disclosed for other purposes with your permission, except as required by law. Your child's information will remain confidential except in the case of a legal requirement to pass on personal information to authorised third parties. This requirement is standard and applies to information collected both in research and non-research situations. Such requests to access information are rare; however we have an obligation to inform you of this possibility

In accordance with relevant Australian privacy laws, you have the right to access the information collected and stored by the research team about your child. You also have the right to request that any information with which you disagree be corrected. Please contact the researchers named at the end of this document if you would like to access your child's information.

What will happen to my child's family history information?

Family history information will be stored along with your child's clinical and genetic information in a secure and confidential database (registry) held jointly by the Children's Cancer Institute and the Sydney Children's Hospital Network. Research results have the potential to influence and inform clinical management. This information may be used for your child's medical management, research purposes and to better understand how cancer predisposition syndromes present clinically. This information may also be important for the healthcare of other relatives in the family. No identifying data will be released or made public.

This information may be useful for your child's future health management. This information may be transferred to a clinical database to assist in your child's management.

Will the study cost me anything?

There are no additional costs associated with participation in this research study, nor will you or your child be paid for participating.

A sub-study that looks at associated costs and benefits of finding a CPS

You can choose whether or not you and your child wish to also take part in this sub-study. There will be an option on the consent form where you can choose for you and/or your child not to participate in this sub-study. If you choose not to, your child can still be part of the main study looking for a CPS.

What is this sub-study doing?

We want to understand the costs and benefits of using genetic testing in everyone diagnosed with a childhood cancer aged 21 or under.

What do I have to do on behalf of my child to take part in the sub-study?

1. Let us use your child's identifying information (e.g. name, date of birth, address) so that we can collect health-related data about them from a range of sources

In these datasets, your child's health information is de-identified (data is made anonymous). This is to ensure their personal privacy is protected. That is why we need their identifying information to be able to access their health information. Being able to access information using these data sources avoids us having to contact you in the future to ask you further questions. The information will be treated completely confidentially and used **only** for the purposes of this research study. The information sources include those held by hospitals, NSW and Commonwealth health departments and other groups or organisations that provide health services or collect health data such as the Cancer Institute NSW.

2. Let us collect your child's Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) data

You will be asked to sign a consent form authorising the study to access your child's complete Medicare Benefits Schedule (MBS) and/or Pharmaceutical Benefits Scheme (PBS) information as outlined in the Medicare and PBS consent form. Medicare collects information on your child's doctor visits and the associated costs, while the PBS collects information on the prescription medications you have filled at pharmacies. The consent form is sent securely to Services Australia who holds MBS and PBS data confidentially.

- Where children under the age of 14 are being recruited, a separate child Medicare and PBS consent form will need to be used. If a child turns 14 years of age during the recruitment process, they will need to complete and sign the Medicare and PBS

consent form themselves. Alternatively, the form can be signed by a power of attorney or legal guardian. A certified copy of any authority to sign on behalf of a child must be provided with the consent form. This may mean some children will require more than one consent form to be completed for the purposes of the study. Please note, adolescents who turn 14 years of age during the study are only required to complete and sign the Medicare and PBS consent form as per Services Australia's policy. This is not applicable to the main study where participants must be 18 years old to consent as per the approving ethics policy.

- Where a child under 14 years of age is on two Medicare cards, both card numbers and the signatures of both primary card holders will need to be on the child's consent form. Data relating to a child's Medicare card will only be supplied where the primary card holder of that card has consented.

Medicare and PBS data collected from Services Australia will be stored on the Children's Cancer Institute secured server, which is physically located within Australian borders, and access to the data will be limited to authorised researchers in this study via assigned login password. Data collected from Services Australia will be securely destroyed within a period of 5 years of the publication of the study's final report, and will not be used for future related or unrelated studies.

Where is the research being done?

The study is a partnership between Sydney Children's Hospital, Westmead Children's Hospital and Children's Cancer Institute supported by research grants from the NSW Ministry of Health's Luminesce Alliance Fund.

What will happen once my child turns 18 years of age?

It is the law that a person who is 18 years of age and older must give their own permission to be part of a research study. Although you may have given this permission to the PREDICT study now, once your child turns 18 years old, the study team may get in touch with them again to make sure they still agree with being part of this research.

Who has reviewed the research study?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research study have been approved by the HREC of The Sydney Children's Hospital Network.

This study will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

Who can I contact if I need further information?

If you would like more information about the study or you need to speak to a member of the research team, please contact:

Clinical contact person

| | |
|-----------|----------------|
| Name | [Name] |
| Position | [Position] |
| Telephone | [Phone number] |
| Email | [Email] |

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Research Governance Officer Details

| | |
|-----------|----------------|
| Name | [Name] |
| Position | [Position] |
| Telephone | [Phone number] |
| Email | [Email] |

If you have any complaints about any aspect of the study, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer Details

| | |
|------------------------|--|
| Reviewing HREC name | |
| Study Reference number | |
| Position | |
| Telephone | |
| Email | |

What do I do if I have a privacy complaint?

If you have a privacy complaint in relation to this study, contact the Office of the Australian Information Commissioner. You will be able to lodge a complaint with them.

| | |
|-----------|--|
| Website | |
| Telephone | |
| Email | |
| Mail | |

Thank you for considering this invitation