

# NeuRA research project

## Genetic contributors, clinical course and pharmacogenomics of Bipolar Disorder

**Overview:** This important research project will use DNA obtained from blood samples to identify the specific genes that contribute to the development of mental illness, and also in what way a person's genes affect how he or she responds to medications. This is known as pharmacogenomics. The project will also examine why people with bipolar disorder tend to have higher rates of physical medical illness (such as cardiovascular disease, diabetes and asthma) than the general population, and how physical health impacts their mental health. The project will combine these outcomes with information about pharmaceutical use and/or visits to hospital, with a long-term goal of better understanding the causes of mental illness, and helping doctors select the treatments best suited for each person to improve quality of life.

**Investigators:** The project is led by Associate Professor Janice Fullerton (Principal Research Scientist at NeuRA), together with Professor Philip Mitchell (UNSW Medicine & Health), and Professor Peter Schofield (NeuRA). The research team at NeuRA and UNSW also includes Ms Bronwyn Overs, Dr Samuel Brennan, Ms Kerrie Pierce, Professor Melissa Green, Dr Alys Havard, Dr Claudio Toma, and Dr Maryanne O'Donnell.

**Project Information:** This project will utilise health-record data, surveys and biological information derived from blood samples obtained from consenting participants to address four knowledge gaps:

1. Identification of genes and molecular pathways that increase risk of bipolar disorders;
2. Pharmacogenomics studies to examine individual genes and genetic signatures which may predict responsiveness to commonly used medicines;
3. Examination of the impact of rare damaging genetic variants on disease severity; and
4. Consideration of the genetic correlates of illness progression, disease severity and relationships to physical health conditions.

**Project Outcomes:** This project will enhance capacity for tailoring treatments to specific individuals, thereby reducing periods of active illness and improving quality of life. This project will also promote the effective recognition and management of physical illness in individuals with bipolar disorders, which may improve how these conditions are treated and lead to improved functional outcomes of patients. Furthermore, it will identify subgroups for whom specific therapies would be most beneficial, enabling faster and better medication response. Ultimately, the implementation of genomic-based screening could constitute a major advancement in the effective treatment and clinical management of bipolar disorder.

**Participant Eligibility:** 45 and Up Study participants who have received a diagnosis from a doctor of bipolar disorder, acute mania, schizoaffective disorder, schizoaffective psychosis or cyclic schizophrenia, and who are willing to provide a blood sample at their local NSW Health Pathology service and complete a questionnaire, are eligible to participate.

**Resources:** If anyone is distressed and needs immediate mental health support, 24 hour crisis support and suicide prevention services are available through Lifeline on 13 11 14 or at <https://www.lifeline.org.au/>

Beyond Blue offers 24 hour support services via phone on 1300 22 4636, webchat (3pm-12am) and email. <https://www.beyondblue.org.au/about-us/contact-us>

For more information about bipolar disorder, its causes and treatments, as well as access to online assessments and clinical resources to help best manage your mental illness, please refer to: <https://www.blackdoginstitute.org.au/clinical-resources/bipolar-disorder>

For more information about the mental health researchers involved in this study, and the work undertaken at NeuRA in the area of bipolar disorder, please refer to: <https://neura.edu.au/health/mental-health/bipolar-disorder>

For more information about the NSW Health Statewide Biobank, please refer to <https://biobank.health.nsw.gov.au>

## Frequently asked questions

### 1. What's involved in providing a blood sample?

A blood sample will be collected by an experienced technician at selected NSW Health Pathology centres. A portion of this sample will be used in this research project for biomarker analysis and/or genetic testing, which may include whole genome sequencing of your DNA. The remainder of your sample will be included in the 45 and Up Study Biobank.

### 2. Why does this research project want to examine DNA?

DNA carries the hereditary information (genes) that underlies the physical and behavioural characteristics of all living beings. DNA is now routinely collected by many studies investigating a range of traits and diseases.

Genetic research tries to identify the genes and genetic variants that may be linked to health measures, traits and diseases.

Analysis of the DNA in your blood sample will allow us to investigate if there are genetic characteristics that influence risk of bipolar disorder, or that could indicate how a person might respond to particular mood-stabilising medicines. This will enable us to better understand the causes of this condition, and the factors that predict good or bad outcomes for patients. This research may potentially lead to the development of diagnostic tests, and novel ways to treat bipolar disorder and other mental illnesses to improve quality of life for patients and their families.

### 3. How will the blood samples be used and stored?

A portion of the collected samples will be stored indefinitely as part of the 45 and Up Study Biobank, supported by NSW Office for Health and Medical Research. Derivatives of the blood samples (such as DNA, RNA, serum) will be used for analysis in this project, with a portion of sample derivatives stored securely at Neuroscience Research Australia (NeuRA). The biospecimens may be sent to third party genomics service providers for analysis. Any sample remaining at the genomics service provider at the conclusion of the service will be destroyed by the provider, or returned to the NeuRA research team.

Samples stored in both the NeuRA Biobank and the 45 and Up Study Biobank will be stored indefinitely and may be used in additional health-related research either nationally or internationally that is in the public interest, only after receiving approval from the 45 and Up Study and an Australian

Human Research Ethics Committee. It is not possible to foresee all the potential projects that may use the genetic material, now or in the future. Researchers may be from non-profit research institutes such as universities or from commercial organisations from Australia or overseas.

Access to samples is granted only after meeting strict guidelines, and with approval of the Biobank Access Committee and the completion of contractual agreements between the researcher's organisation and the NSW Health Statewide Biobank. This committee will be required to meet Australian ethical standards.

The storage and use of all genetic material will be conducted in accordance with the National Health & Medical Research Council's Guidelines for Genetic Registers and Associated Genetic Material (1999), the Human Tissue Act (1984, amendments 2003), the National Statement on Ethical Conduct in Human Research (2007) and relevant Australian Legislation.

#### **4. What is a biobank?**

A biobank is a collection of human biological samples or 'biospecimens' (e.g. blood, saliva, tissue etc.) and/or their products (e.g. DNA, serum).

Like a bank, samples donated for health and medical research are kept under tight security and in carefully controlled conditions.

Samples are stored securely, together with samples from many other people, for use in ethically approved health and medical research projects, now and into the future. Storing samples together allows researchers from across NSW and Australia to work together to find new or better treatments for illness and disease.

The NSW Health Statewide Biobank is a secure NSW Government facility. It's the largest facility of its kind in the Southern Hemisphere and uses robotic technology to store and process millions of biospecimens to support health and medical research.

The Biobank provides approved researchers with access to a range of human samples and linked health data to help them better understand, detect and treat illness. You can find more information at [biobank.health.nsw.gov.au](http://biobank.health.nsw.gov.au)

#### **5. What does it mean to participate in a biobank?**

Your participation in the biobank is voluntary, however, the NeuRA research project will operate through the NSW Health Statewide Biobank and all samples received for this research project will contribute to the 45 and Up Study Biobank.

If you do not want your sample to be stored in the biobank, please do not participate in this research project. If you agree to participate and have completed the consent form, a portion of your donated blood sample will be biobanked as part of the 45 and Up Study Biobank.

Your choice to donate a sample and allow access to your health and personal information will support research that could result in discoveries that could change, improve and save the lives of others in the future.

#### **6. What does it mean to consent to biobanking?**

Consenting to biobanking means you are also consenting for researchers to access and link information held by other organisations. This is called data linkage, and is part of being a participant in

the 45 and Up Study. This health information may include details about your operations, diagnosis history, pathology results, hospital records and genetic or family history details. Your health information may be linked with other personal information held by the 45 and Up Study (e.g. education, employment status, lifestyle factors).

You are also consenting to be notified of incidental findings. For further information on the significance of this decision, please refer to questions 14-17.

If you decide to participate in biobanking, you are encouraged to tell your family of your decision and why you chose to support health and medical research in this way.

By consenting to link your biological sample with your health and personal information, you are providing a valuable resource for future health and medical research that is in the public interest. This will only occur with approval from a Human Research Ethics Committee.

While your sample may contribute to research that has a commercial benefit, for example the development of a new technology, you will not be entitled to receive a financial return.

## **7. What does data linkage mean?**

Record or data linkage brings together information that relates to the same individual from different data sources. This linked data helps researchers better understand people's health journey, which can improve treatment and health services delivery. For more information on how data linkage works see <http://www.cherel.org.au/how-record-linkage-works>

Data linkage helps researchers to better understand health and healthcare over a person's life. Linked data can help us to understand how lifestyle, medications, treatments, genes or other factors might affect future health in the population. It can also help to improve the delivery of healthcare, develop future treatments and even cures.

## **8. Who is responsible for my biobanked samples?**

The NSW Health Statewide Biobank will be responsible for storing the samples. Access to and use of all samples in the 45 and Up Study Biobank will be governed by the Biobank Access Committee, and only provided for use in research to authorized researchers with approval from a Human Research Ethics Committee.

## **9. What will happen to my data?**

All personal data will be stored using strict privacy protocols and in accordance with NSW Government requirements. All research using biospecimens and linked data must have ethical approval.

Researchers are only provided information without identifying personal details (e.g. your name and address). In the event of an incidental finding (see questions 14-17), the 45 and Up Study will follow its established protocols to reidentify you if required.

## **10. How will my privacy be protected?**

Identifying personal information (e.g. name, address) will be removed from your samples and replaced with a unique number for research purposes. Your sample will be stored indefinitely in this way.

Your identifying personal information will be kept by the 45 and Up Study, and will be kept separately to your biobanked sample. Your personal information will be retained by the 45 and Up Study for the duration of the Study plus a further period as defined by the Study's ethical approvals.

The information you provide in the questionnaire and consent form will also be kept by the NeuRA researchers. Personal identifying information will be kept separately to any genetic information, and retained for the duration of the study plus a further period as defined by ethical approval (typically seven years after study completion).

There may be instances where genetic information obtained from donated samples may lead to the identification of participants, but this is highly unlikely (for example, if genetic information derived from your sample is matched to previously stored genetic information and identifiers of yours). The biobank requires this genetic information to be kept strictly confidential and there are legal requirements for researchers to maintain your privacy.

### **11. Will my samples and data only be used for Australian based research?**

It is common in health and medical research for international and interstate-based researchers to collaborate. If you agree to participate, your samples and associated information may be sent interstate or overseas for collaborative research purposes. This will be done in such a way that you cannot be identified, and only after a Human Research Ethics Committee (or an international equivalent that meets Australian ethical standards) has approved the research. Approved researchers will only have access to your samples (and research results obtained from your samples), not your identifying personal information. Collaboration helps to speed up the time it takes to translate research lab discoveries into better patient care.

### **12. Can anyone other than the 45 and Up Study and approved researchers access my biobanked sample?**

There may be circumstances where it is a legal requirement to provide information about your biobanked sample outside of approved health research projects. While these situations are rare, the 45 and Up Study and the NSW Health Statewide Biobank will be required to comply with their legal requirements and make this information available.

### **13. What if I change my mind later and want to withdraw my consent?**

Participation in biobanking is entirely voluntary. Even after you have provided the 45 and Up Study with your sample, you are free to withdraw all, or part of, your consent at any time without having to give a reason, by contacting the 45 and Up Study. Choosing not to participate, or withdrawing your consent to participate, will not affect your medical treatment in any way.

Should you choose to withdraw your consent, the 45 and Up Study will discard your stored biobanked sample. However, if some or all of your biobanked sample has been provided to a research project, it will not be possible to retrieve these samples.

Also, research that has been published cannot be deleted or discarded, but you will not be able to be identified in any way.

#### **14. What happens if serious health implications (incidental findings) are discovered in my sample?**

Very rarely when tests are done on donated samples, a potentially serious and important piece of information can be discovered. For example, a change in your DNA could indicate a higher risk of a heart problem. This DNA might be something you share with your genetic relatives, such as your parents, siblings or children. **These findings happen when a researcher discovers something potentially serious about your health that they weren't specifically looking for and are known as incidental findings.** Only findings that are of a highly serious nature will be returned to you, such as the identification of a gene for sudden cardiac death. General health information, such as evidence of elevated risks for high cholesterol or diabetes, will not be returned.

In the consent form we ask you to agree to be contacted by a doctor or healthcare professional about a potentially serious incidental finding.

If you are not contacted to advise you of an incidental finding, this does not mean that you do not have any health issues. It is important to continue any regular clinical check-ups, as researchers do not perform screening on your sample during their research.

In the rare event that an incidental finding is discovered, the 45 and Up Study will refer the matter to a clinical expert, who will evaluate the result to determine whether it is a serious and significant finding and whether it should be returned to you for further action. This may involve further tests, genetic or otherwise, to ensure the validity of the finding.

#### **15. How and when would I be told about serious incidental findings in my sample?**

Consenting to biobanking means you are consenting to being contacted in the unlikely event that a potentially serious incidental finding is found by a researcher during the course of their research. If this occurs, you may be asked to provide a second blood sample for confirmatory testing.

You would only be contacted about potentially serious findings if they meet each of the following criteria:

- **Significant:** The finding indicates a potentially life-threatening health condition or affects your reproductive health.
- **Actionable:** There are specific established treatments or other available actions that might help you.
- **Confirmed:** The finding has been checked as accurate and/or valid, as far as reasonably possible within a research context and to current best knowledge.

#### **16. Why am I being contacted about a serious finding, and what are my options?**

Being informed of incidental findings might benefit you by giving you early access to treatments to improve your health and wellbeing, but might also have negative implications for life insurance cover for you and your blood relatives.

If you are contacted about a potential serious finding, but you do not wish to be told details, see a medical expert or undertake further testing, you do not have to. However, even if you don't agree to be told details about your serious finding, in rare cases, if there is a serious and imminent threat to health, the 45 and Up Study may contact you or your nominated contact person or next of kin to provide further information.

As some incidental findings may have impacts on your genetic relatives, we encourage you to inform them of your participation in the biobank. After further testing, this information may become part of your health record as health information.

If a serious finding is made and you are told about it, it might have an effect on any insurance you apply for in the future (for example life insurance or income protection). We suggest you get advice from your chosen insurer.

### **17. Could taking part impact my ability to take out health or life insurance in the future?**

In rare cases, taking part in health and medical research might affect health or life insurance cover for you and your blood relatives. For example, if you have a serious and life-threatening genetic condition that you share with your family, it could affect insurance you apply for in the future (for example life insurance or income protection).

Currently in Australia, genetic research does not affect your ability to obtain private health or life insurance. It is however possible that in the future, the fact that you have taken part in a study involving genetics might affect you or your family if you want to take out a new health, disability or life insurance policy. We will not pass on any information about you to anyone, including your family members, without your written permission unless obliged to by law.

A downloadable fact sheet about genetic tests and life insurance prepared by the Financial Services Council is available at [fsc.org.au/resources/1785-moratorium-key-facts](https://www.fsc.org.au/resources/1785-moratorium-key-facts)

### **18. What should I do if I have further questions about my involvement in the research project?**

If you require further information regarding this research project, please call the 45 and Up Study Infoline on 1300 45 11 45 or email [45andUp@saxinstitute.org.au](mailto:45andUp@saxinstitute.org.au)

If you need to contact the NeuRA research team, please phone (02) 9399 1166 and leave a voice message, or email questions or concerns to [neura45andup-substudy@neura.edu.au](mailto:neura45andup-substudy@neura.edu.au)

Please note that contacting the NeuRA research team directly may disclose your participation in the 45 and Up Study to NeuRA researchers. Your name and contact details will be treated confidentially, and will not be linked by the NeuRA research team to any health or personal information which is held by The Sax Institute about you, which will always remain confidential.