The PICOBOO study Adolescent and Parent/Guardian participant information sheet

The Platform Trial In COVID-19 Vaccine priming and BOOsting, a single blinded, phase IV, adaptive randomised control trial to evaluate the comparative effectiveness of COVID-19 booster vaccines

Coordinating Principal Investigators: Professor Peter Richmond and Dr Charlie MacLeod
Sponsor: Telethon Kids Institute (TKI)

We are undertaking research involving COVID-19 booster vaccination, which is why we have approached you/your child.

You/your child are/is invited to take part in this study, but before you/ your child decide whether you/your child to take part, it is important for you/your child to understand why the research is being done and what is involved.

Please take time to read this information carefully. Please ask us if there is anything that is not clear, or if you would like more information or time to decide. Taking part is completely voluntary. You/your child will need to agree to take part for participation to occur. The decision you make **will not** affect your/your child's access to health services or other aspects of your/your child's health care in any way.

Participation in this study could make a difference to optimising our control of the COVID-19 pandemic. Thank you for reading this information leaflet. A copy of this document will be given to you to keep. Your help, whatever your final decision, is very much valued.

What is the study about and why are we doing it?

While booster vaccines are approved for use in Australia to protect us against COVID-19, many unanswered questions remain about the best strategies for vaccine boosting. These questions include how vaccination impacts on different aspects of the immune system, how long immunity lasts, and whether optimal boosting strategies differ depending on age and previous receipt of COVID-19 vaccines.

To answer these questions, researchers across multiple sites within Australia will work together to conduct a clinical trial to generate high-quality evidence to inform vaccine practice and policy in Australia.

What is involved if you/your child choose to take part in this study?

To take part in the study you/your child will need to have received primary COVID-19 vaccination (two doses). If you/your child takes part in this study and you/your child provides consent, you would be agreeing to take part in the following study procedures:

- We will collect background information about you/your child including your/your child's age and ethnicity, and any medical conditions you/your child may have. With your/your child's permission, we will also request relevant health records from other providers (for example your General Practitioner or if you/your child are/is admitted to hospital).

- Be randomly allocated to receive a COVID-19 vaccines. The vaccine you/your child are allocated to will be chosen at random by a computer. You/your child will have an equal chance of receiving:

  Pfizer Comirnaty (Bivalent)
  OR
  Moderna SpikeVax (Bivalent)
  OR
  Novavax Nuvaxovid

- Undergo blood tests before and at pre-specified time points after the booster vaccination to measure your/your child's immune response to the vaccine and how long it lasts for. We will collect approximately 50mL of blood at the following time points:
  - Visit 1: Prior to receipt of booster vaccine
  - Visit 2: 1 week after vaccination
  - Visit 3: 1 month after vaccination
  - Visit 4: 6 months after vaccination
- Give saliva samples (~ 2mL) at Visit 1, Visit 3 and Visit 4
- Undergo an additional blood and saliva test if you/your child are/is diagnosed with COVID-19 infection during the study, at least 7 days after confirmed infection or upon completion of quarantine isolation to see if this has boosted your/your child's immunity.
- You/your child will be provided with a thermometer to measure your temperature, a tape measure to assess any reactions that may occur at the site of booster vaccination, and a memory aid to record them. Every day for 7 days after vaccination, at approximately the same time of day as your COVID-19 vaccine dose, you/your child will be required to measure and record your/your child's temperature, as well as any swelling or redness at the injection site. You/your child will also be required to measure and record your/your child's temperature if you/your child feel feverish (feeling cold or shivery) at any other time in the day and record in the memory aid.
- Complete short (2-5 minute) surveys via SMS (short message service) or in-person (or over the phone if required):
  - Daily until 7 days after COVID-19 booster vaccination to report any reactions that occur. Every day you or your parent/guardian will receive an SMS survey to check your/your child's maximum temperature in past 24 hours and whether you/your child had any swelling or redness at the injection site.

- At 1 month to see if you/your child developed any new medical conditions or went to hospital
- 3 monthly up to 2 years to determine if you/your child have/has been diagnosed with COVID-19 infection, hospitalised for management of COVID-19 or you/your child have taken time away from school/work/normal activities because of COVID-19 infection.
- A follow-up phone call by a research team member may be received if required.

We will send a letter to your nominated GP to ask them to notify us of any confirmed COVID-19 infections or hospitalisations due to COVID-19 infection that occur during the study period.

If you/your child choose to take part, you will not know which COVID-19 booster vaccine will be given. This is to make sure that the different COVID-19 vaccines can be compared fairly. The specific vaccine you receive will be uploaded to the Australian Immunisation Registry (AIR) 6 weeks post vaccination. If you/your child requires detailed proof of vaccination for visa, education, employment or travel purposes, your/your child can request this information earlier from the study team.

We are also asking permission to store any residual blood samples to test your blood in the future to look at other aspects of you/your child's immune response to the vaccines or infection.

We will additionally seek permission to contact you/your child in the future to consider participating in additional COVID-19 research, including further COVID-19 booster vaccination studies, if regular COVID-19 boosters become necessary.

Who is suitable to take part?

To be eligible to take part in this COVID-19 booster study, you/your child must be ≥12 years of age and have received two doses of a COVID-19 vaccine (either two doses of Pfizer or two doses of Moderna vaccine) and be willing to take part in all the study procedures mentioned above, including receiving a COVID-19 booster vaccine, undergoing blood tests at Perth Childrens Hospital within the specified time intervals. You/your child must also be willing to complete the study surveys.

Which vaccines are being used in this study?

Vaccines used in this trial will be approved (including for emergency use) to prevent COVID-19 disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in the intended age group by the Therapeutic Goods Association (Australia), or by an equivalent regulatory agency.

In instances where a specific vaccine is not approved for the specific indication within a defined age cohort by the TGA (e.g., for primary vaccination but not booster vaccination), the vaccine will be studied under a clinical trial notification (CTN) and appropriate ethics approval.

Please note, evidence for COVID-19 vaccination is rapidly evolving and we recommend you discuss the latest approved age groups for COVID-19 vaccination boosting in Australia as per the Therapeutic Goods Administration (TGA) and the Australian Technical Advisory Group on

Immunisation (ATAGI) with a member of our research team prior to enrolment in this study. You can also discuss this with your usual GP.

The vaccines available for use in this study are Pfizer Comirnaty vaccine Bivalent (Pfizer), Novavax Nuvaxovid (Novavax), or Moderna SpikeVax Bivalent (Moderna). Vaccines used for this study will be dependent on local availability. You/your child can find out which vaccines are available at your location from the study staff. All vaccines used in this study are approved as safe and effective for preventing COVID-19 by the TGA of Australia, however, some vaccines might not be approved in Australia as a booster dose in adolescents ≥12 years of age, so please discuss the latest recommendation and where this differs with the study team.

There is data to suggest that the Pfizer, Novavax and Moderna COVID-19 vaccines (including the bivalent vaccines) are safe and effective when delivered as a *booster* vaccination in adults for those who have previously had two doses of a COVID-19 vaccine. While children less than 16 years of age are not universally recommended to undergo a booster vaccination in Australia, currently, children >12 years of age with risk factors for severe disease are recommended to undergo booster vaccination with Pfizer or Novavax. The Moderna bivalent vaccine is currently recommended for adolescents >12 years of age by the European Medicines Agency (EMA), but not yet in Australia There is a need to compare these vaccines 'head- to-head' in well-designed clinical trials to determine which vaccine(s) offer the greatest protection for adolescents against SARS-CoV-2, in order to shape Australia's vaccination strategy, moving forward.

If you take part in the study, you/your child will receive one injection. After booster vaccine/dose, you/your child will be watched for at least 15 minutes in case of a rare anaphylactic reaction following the administration of vaccines.

What will happen to your/your child's information?

All data collected will be entered electronically and stored on a research database named REDCap (Research Electronic Data Capture). This is a secure, web-based, non-commercial, data management tool designed for research purposes, hosted and backed up on the Telethon Kids Institute server. No personnel other than the researchers will have access to the research documents. The data will be analysed by members of the research team.

All data for use in journal publications and presentations will be de-identified. This means that it will not be possible for you/your child to be personally identified based on the information presented. The files will be retained for 25 years from the day the study is completed. Once this retention period expires/lapses, identifying information will be disposed of using the Telethon Kids Institute disposal service. The data may be used for future research purposes; however, Human Research Ethics Committee (HREC) approval will be sought prior to any future use of the data. Text message surveys for this study utilise a third-party service called Twilio. SMS messages are routed through Twilio's servers which are based in the United States; however, these messages are removed from the Twilio server shortly after they are sent to ensure safety and privacy requirements (in accordance with the Health Insurance Portability and Accountability Act) are met.

What will happen to your/your child's blood and saliva samples?

You/your child's blood and saliva samples will be de-identified (your name removed and replaced with a unique code). The saliva samples will be processed, and blood samples will be separated in the laboratory into different components. Samples will then be shipped to and stored at specified collaborating laboratories in Australia for up to 25 years. You/your child's samples or data may be sent overseas or given to a third party with your permission. This may be required for collaborative research or local and international regulatory approvals. All additional research will have prior ethics approval.

What tests will be performed on me/my child's blood samples and saliva?

We will measure the level and type of antibodies and immune cells your/your child's body produces against COVID-19 before and after you/your child receives your/their COVID-19 booster. Residual blood samples and saliva will be stored securely in one of the affiliated laboratory facilities to allow additional immunological studies to be conducted in the future to determine how booster vaccines impact on the immune system. Further approvals from the ethics committee will be sought prior to any additional testing being performed that is outside the scope of this study.

We will also test your/your child's bloods samples to assess if you/your child have/has been infected with COVID-19 during the study period. You/your child will be notified of any positive results via email, if this occurs.

Will genetic tests be performed on me/my child's samples?

Genetic material will be extracted and used to do special genetic tests to evaluate susceptibility to and protection from SARS-CoV-2 by cellular immunity. However, we are not looking for specific genetic or hereditary defects that might predict the future health of you/your child, your family members or your community. We may generate results that could be predictive of your/your child's future health, but your/your child's identity will be removed, and we will not link the results back to you/your child or return the results of any genetic analyses. However, your/your child's DNA is unique so it can never be completely anonymous.

Are there any benefits to taking part in this study?

We expect that by receiving a COVID-19 booster vaccine you/your child will be better protected against COVID-19, but the extent and duration of this protection is unknown. There will be no other benefit to you/your child.

Results from this study will be valuable in informing the national and global response to the COVID-19 pandemic and help us determine the optimal COVID-19 booster vaccination strategies within Australia.

Compensation will be provided for the time and resources (e.g. parking and travel costs, time away from work) spent in completing the study procedures. This includes $100 for visit 1 (which may take up to two hours) and $65 for visit 2 – 6 (which should take less than one hour).

What are the risks of being in the study?

All Australians ≥16 years of age are recommended to receive a mRNA COVID-19 booster vaccine to protect them against COVID-19. Potential vaccine-related adverse events include injection site reactions (redness, swelling, pain and hardness) and fever, muscle aches, and malaise (feeling 'under the weather'). Most side-effects are mild and last 1-3 days.

A small increased risk of myocarditis (inflammation of the heart) or pericarditis (inflammation of the tissue surrounding the heart) has been observed in people who have received Pfizer Comirnaty or Moderna Spikevax vaccine, compared to unvaccinated people. This has been reported most in males under 30 years of age, usually after the second dose of vaccine and is less common after boosters. COVID-19 infection itself is associated with a much higher risk of myocarditis and other cardiac complications compared to vaccination. Symptoms of myocarditis or pericarditis usually appear 1-5 days after vaccination and include chest pain, palpitations (irregular heart rate), fainting or shortness of breath. If this occurs, you/your child should seek medical attention and notify the research team.

Trials of Novavax Nuvaxovid in adolescents have not suggested any major adverse events of concern, however further evidence is required to establish the safety profile in this age group. We will monitor your/your child's reactions daily in the 7 days and at 1 month after your/your child's vaccination.

With any vaccination there is a small risk of rare serious adverse events, such as an allergic reaction. These may be related to the immune system or to the nervous system. Severe allergic reactions to vaccines (anaphylaxis) are rare (approximately 1 per million vaccine doses) but can be fatal. In case of this unlikely event, medication for treating allergic reactions is available and the researchers are appropriately trained in the management of anaphylaxis.

If you receive a booster vaccine ahead of national recommendations (e.g. if you receive a 3rd booster before recommended by ATAGI) as part of the PICOBOO study, this may preclude you from receiving another government funded vaccine when a recommendation is made. If this occurs and our medical team believe you may have reduced protection against COVID-19 due to the time since your last booster, we will ensure you are able to receive an additional vaccine

We are collecting personal information about you/your child and your/their health, so there is a small risk of an accidental breach of your/their privacy. This will be minimised by removing

information that could identify your/your child personally wherever possible, and by storing your/your child's information in a secure, password protected database with access limited to authorised research staff.

Blood sampling will cause temporary discomfort but the amount of blood to be taken is unlikely to cause symptoms. The maximum volume of blood to be collected at a single visit is 50mL and is unlikely to cause anaemia. There may be slight bruising at the site where the blood was taken, however this is unlikely to persist beyond a few days. Taking blood may sometimes cause fainting or a feeling of 'light-headedness'.

What happens if an adverse event following immunisation (AEFI) occurs?

If you/your child experiences an adverse event following immunisation (AEFI), it is recommended that you/your child seek medical review, if required, through your/their usual health care channels (such as via a General Practitioner) or local Emergency Department if urgent medical care is required. AEFIs should be reported to the relevant authority for each state. Please contact the study team on 0400 450 240 if you experience an AEFI and we will ensure it is appropriately reported.

What should I do if I think my child may have COVID-19 during the trial?

A common and expected side effect of COVID-19 vaccines is fever. If you/your child develop a fever in the first 48 hours following vaccination, you will not need to self-isolate, unless you/your child have/has other symptoms of COVID-19. If you/your child's fever continues (or you/they have another episode of fever) after 48 hours, then you/they will need to follow the current government advice. We also ask you/your child to record any fever on your/their memory aid and/or the SMS survey. If the fever doesn't continue, then it is likely that it was a vaccine effect, and you/they can carry on as normal.

If you/your child develop symptoms that meet local department of health COVID-19 testing criteria, then you/your child must arrange a COVID-19 test as soon as possible, following the normal routes. **IF YOU/YOUR CHILD TESTS POSITIVE TO COVID-19 INFECTION DURING THE COURSE OF THE STUDY, WE ASK YOU TO NOTIFY A MEMBER OF THE STUDY TEAM** on 0400 450 240. After hours, please phone 08 6456 2222 and ask to be put through to the on-call staff member for Vaccine Trials Group. Rapid COVID-19 tests (e.g., rapid antigen tests) may be supplied directly to you/your child by a member of the research team to facilitate rapid testing for COVID-19 if you/your child become symptomatic during the trial. If you/your child's test positive on a rapid COVID-19 test, we would also like you/your child to present to your local COVID clinic for a polymerase chain reaction (PCR) test. This involves collecting a nasal swab.

If you/your child develop confirmed COVID-19 infection during the study, we will ask you/your child to come in for an additional blood and saliva sample after you/your child finish(es) the isolation period.

If you have a copy of your/your child's COVID-19 results, we ask you to please forward a copy of these results to us. If you/your child are/is diagnosed with COVID-19 during the study, you /your child will be required to follow usual infection control and isolation precautions as per local policy.

Who is responsible and what if something goes wrong?

The research is sponsored by the Telethon Kids Institute (TKI) and is being conducted in collaboration with researchers based at the University of Sydney, the University of Melbourne, the Royal Melbourne Institute of Technology, the University of Adelaide and the University of Tasmania. Participating recruitment sites include the Vaccine Trials Group in WA, Launceston General Hospital, Launceston Medical Centre, Melbourne Children's Research Institute, Monash Health and the Women's and Children's Hospital in Adelaide. None of these institutions will benefit financially from the study.

Each participating trial site is protected by their own indemnity insurance arrangement. TKI has arrangements in place to provide for any harm arising from participation in the study for which it acts as the Research Sponsor. If you/your child wish to complain about the way in which you/your child have/has been approached or treated, or how your/your child's information is handled during this study, you can/your child can contact Director, Governance & Risk on (08) 6319 1659 or the research study team on 0400 450 240.

Compensation for injuries or complications

If you/your child suffers any injuries or complications because of this study, you/your child should contact the study doctor as soon as possible, who will assist you/your child in arranging appropriate medical treatment. If you/your child are/is eligible for Medicare, you/your child can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

Does my child/do I get access to extra medical treatment from being in the study?

If you/your child become unwell and needs to be admitted to hospital, the standard referral routes within your/your child's local health system will be used. We are unable to offer extra medical support outside what is available within your/your child's local health system for the general public.

If you/your child are/is admitted to hospital during the study, then you/your child should inform the study team as soon as possible.

Can I request that I/my child be withdrawn from the study at any point?

Yes, you or your parent/guardian can withdraw at any time without giving a reason and without affecting your/your child's current or future care.

If withdrawal occurs because you/your child have/has experienced intolerable side-effects, you/your child will be provided with medical care until the condition becomes stable and returned to the care of your/their general practitioner. If the medical care team or general practitioner require information regarding the study, they may contact the study team on 0400 450 240.

If you/your child withdraw(s) from the study, you/your child will be able to find out what booster vaccine you/your child received via the MyGov website ~6 weeks after booster administration. If you/your child have/has already provided blood samples for the study at the time of study withdrawal, you/your child may request they be destroyed if they have not already been tested. If you/your child withdraw(s) from the study, the study staff will not collect any more personal information from you/your child, although information already collected will be kept so that the results can be measured properly, and to comply with the law. Please know that information collected up until the time you/your child stop(s) being in the study will be used in the study results. If you/your child do not want the researchers to do this, you/your child must tell them before joining the study.

What about future research?

If you/your child agree to participate in this study, your/your child's information will be used to inform future clinical trials as part of the PICOBOO research project platform.

With your explicit consent, we would like to keep your/parent/guardian's contact details after your/your child's participation in this study is complete, so we may inform you/your child of opportunities to participate in future COVID-19 and vaccine research. This is entirely optional and agreeing to be contacted does not oblige you/your child to take part in any future research.

Your/your child's contact details would be stored securely at Telethon Kids Institute and only authorised study staff will have access to it. We will also retain the consent form if you/ your child are willing to be approached. You can ask us to have your/your child's contact details removed from our database at any time.

Residual blood and salivary samples that are collected will be securely stored for future COVID-19 related research. Further approvals from the ethics committee will be sought prior to any additional testing proposed outside the scope of this study.

What if I would like further information about the study?

If you/your child would like more information about the study, you/your child can contact the research study team on 0400 450 240.

A summary of all results from this study will be made publicly available. These results will not contain information that could allow individual participants to be identified. If you/your child participates and you/your child would like to be informed of the study results, you/your child can indicate so on the consent form and we will contact you/your child with a summary of the study results at the end of the study. You/your child will not be told about your personal immune response.

Is it compulsory to take part in this study?

Participation in any research project is voluntary. If you/your child do not wish to take part, you/your child do not have to. If you/your child decide to take part and later change your mind, you/your child are free to withdraw from the project at any stage.

Your/your child's decision as to whether to take part or not take part, or take part and then withdraw, will not affect your/your child's routine treatment, your/your child's relationship with those treating you/your child or your/your child's relationship with participating research institutions.

Ethics Approval and complaints

All research in Australia that involves humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). This research project has been approved by the Child and Adolescent Health Service Human Research Ethics Committee. This project 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.

If you/your child have any concerns or complaints regarding this study, you/your child can contact the Executive Director Medical Services at Perth Children's Hospital (08 6456 2222). Your/your child's concerns will be drawn to the attention of the Ethics Committee who is monitoring the study. Alternatively, you/your child can email [cahs.ethics@health.wa.gov.au] (project number RGS0000005222).