Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Title	Multicentre Randomised Double-Blind Placebo Controlled Trial of Combination Vancomycin and Cefazolin Surgical Antibiotic Prophylaxis
Short Title	Australian Surgical Antibiotic Prophylaxis (ASAP) Trial
Project Sponsor	Monash University
Coordinating Principal Investigator	Dr Trisha Peel
Principal Investigator	Prof Richard de Steiger
Location	Epworth HealthCare
HREC Number	HREC/18/Alfred/102
Local Project Number	EH2018-358

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you are undergoing surgery. As part of usual or "standard of care" at the time of surgery, you will be given an antibiotic called cefazolin, to help prevent you from developing an infection of your surgical wound. This research project aims to see if giving a second antibiotic called vancomycin, in addition to cefazolin, is better at preventing infections of your surgical wound compared to cefazolin alone.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want 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 to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

At the time of your surgery, your anaesthetist or surgeon will give you an antibiotic called cefazolin through a needle in a vein to help prevent infections involving your surgical wound. This is recommended for patients undergoing joint replacement surgery as part of "standard" care.

Infections of the surgical wound are uncommon (less than one in twenty people undergoing surgery will experience a wound infection) however these infections need to be treated with antibiotics and sometimes people need to be readmitted to hospital and / or to undergo further surgery or procedure(s) to treat the infection.

This study aims to find out if giving a second antibiotic, vancomycin, at the same time as the cefazolin, is better for preventing these wound infections.

Vancomycin is a commonly used antibiotic and is approved in Australia for patients undergoing surgery to prevent infections of the surgical wound. Some research suggests that adding vancomycin to cefazolin at the time of surgery decreases the risk of infection of the surgical wound and also other infections following surgery, such as pneumonia. At present, we do not know if giving vancomycin, in addition to the cefazolin, is better than giving cefazolin on its own.

Also we do not know whether giving vancomycin in addition to cefazolin may cause more side-effects, such as kidney problems, or cause the development of resistant bacteria in the body. We need to undertake this study to find an accurate answer.

This research has been initiated by the study doctor, Dr Trisha Peel, and has been funded by the National Health and Medical Research Council.

This research is being conducted by the Department of Infectious Diseases, Monash University.

3 What does participation in this research involve?

Participation in this study will not require alterations to your surgery or care after surgery. You will be participating in a randomised controlled research project. You will be required to sign the consent form before any study assessments are performed.

Sometimes we do not know which treatment is best for preventing a condition. To find out, we need to compare the different treatments. To do this best we put people into groups and give each group a different treatment. The results are then compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random, like tossing a coin). Along with the standard of care dose of cefazolin you will be randomly allocated to be given either a dose of vancomycin (1.5g) or a placebo at the time of your surgery. A placebo is a medication with no active ingredients or a procedure without any medical benefit. It looks like the real thing but is not.

You will be participating in a double-blind study. This means that neither you nor your study doctor will know which treatment you are receiving. However, in certain circumstances your study doctor can find out which treatment you are receiving. This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way.

After your surgery, if you become unwell for any reason, you will receive appropriate care according to normal standard practice. We will collect information relating to your participation in the study.

A research nurse will visit you regularly until you are ready to go home. They will also contact you by telephone at about one month, three months and six months following your surgery to ask you some questions about any complications you may have experienced.

We will also ask you to answer a short questionnaire about your current quality of life, using a questionnaire called the EQ-5D-3L. This questionnaire consists of five questions about your mobility, personal care, activities, discomfort or pain and your current mood.

We may need to look at your medical record while you are in hospital and after you have gone home, to see if you have had any complications. If we are unable to contact you, we will check with your other doctors for this information.

There are no additional costs associated with participating in this research project, nor will you be paid. All medication, tests and medical care required as part of the research project will be provided to you free of charge.

It is desirable that your local doctor be advised of your decision to participate in this research project. If you have a local doctor, we strongly recommend that your inform them of your participation in this research project. This may be done by your Principal Investigator by providing a letter of support at the time of your enrolment to be given to your local doctor. This will not be done without your permission.

Staphylococcus Carriage Sub-Study

Staphylococcus (such as *Staphylococcus aureus* or "Golden Staph") is a bacteria that commonly occurs on people's skin as part of their normal skin "flora". Following surgery, these bacteria are a common cause of infections of the surgical wound. The purpose of the Staphylococcus Carriage sub-study is to assess whether the effect (if any) of the addition of vancomycin is observed in all patients or only those patients that carry this bacteria on their skin at the time of surgery. In order to assess this, we will take one swab at the pre-admission clinic or day of surgery from two sites (two swabs in total): the inside of your nose and groin ("perineum"). The collection of the swabs, as described is an optional component of the research, if you wish to participate in the Staphylococcus Carriage Sub-Study, you will be asked to sign the separate consent form on page 2 of the PICF Consent Form.

Data linkage component

The purpose of data linkage is to assess how participants in the ASAP study use health services. No information that is collected is used outside the project and therefore will not affect any information held with any health or public services, such as Centrelink.

We wish to use your personal details so we can record whether you saw a doctor after having your surgery. We will request service usage data from the health service authorities which we will match to your personal information, including data from the Victorian Department of Health and Human Services (specifically the Victorian Data Linkages unit) and the Australian Government Department Human Services.

We will be asking for information about whether you saw a doctor after having your surgery as part of the study from Medicare Benefits Schedule (MBS) and whether you had any additional medications, such as antibiotics, and picked them up from a pharmacy from Pharmaceutical Benefits Scheme (PBS). We will ask them details about your medications that you have been prescribed and their cost.

You will be asked to sign a separate consent form for MBS and PBS information Services (a separate consent form to the one used for general participation in this study,). This consent form will be retained by the hospital where you are undergoing your surgery. Only information used needed to identify you will be sent to other agencies, and the information will be provided in a secure and confidential way. This information may include: Medicare number, first name, surname and middle initial, date of birth and gender. The consent form is sent securely to the ASAP co-ordinating site at the Alfred who then sends it to the Victorian Department of Health and Human Services and the Australian Government Department of Human Services who hold this information confidentially.

Study Schedule
There are no extra visits to the hospital required for this study. The schedule for assessments are as follows:

Time of Assessment	Assessments
Pre-admission clinic	Baseline health information Questionnaire (EQ-5D-3L) about your current quality of life Swabs for Staphylococcal Carriage Sub-Study**
In hospital	Information about the operation and any complications experienced
Day 30	Phone call for information about any complications experienced Questionnaire (EQ-5D-3L) about your current quality of life
Day 90	Phone call for information about any complications experienced Questionnaire (EQ-5D-3L) about your current quality of life
Day 180	Phone call for information about any complications experienced Questionnaire (EQ-5D-3L) about your current quality of life
** Only in participants who have consented to the sub-study	

4 Other relevant information about the research project

In total, there will be 4,450 participants taking part in this study from 8 hospitals in 3 states across Australia. This project involves researchers from four universities working in collaboration: Monash University, The University of Melbourne, The University of Queensland and The Queensland University of Technology.

5 Do I have to take part in this research project?

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

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Epworth HealthCare

6 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. If you decide not to participate you will still receive cefazolin as part of your routine care. In addition, you may still also receive vancomycin as part of routine care depending on your doctor's decision.

You can also discuss the options with your local doctor, before you decide whether or not to take part in this research project.

7 What are the possible benefits of taking part?

There will be no clear benefit to you from your participation in this research; however, this research project may help answer a very important question about the best way to prevent infections of the surgical wound.

8 What are the possible risks and disadvantages of taking part?

Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

Vancomycin is a commonly used antibiotic. Side effects from this antibiotic are uncommon, are usually mild and are short lived.

Uncommon side effects occur in less than 1 in 100 people, are usually mild and are short lived including:

- Irritation at the injection site
- Nausea, vomiting or mild diarrhoea
- Dizziness
- Flushing

In very rare cases (less than 1 in 1000), and when patients receive multiple doses of vancomycin (for treatment of an infection for example), - more severe side effects may occur. As the ASAP trial involves the administration of a single dose of vancomycin, the risk of severe side effects is extremely rare. Again these side effects are usually short lived and include:
Allergic reactions

- Kidney problems
- Decrease in the white cell count
- Reversible hearing loss or ringing in the ear. (in most cases reported, patients already had kidney impairment or pre-existing hearing loss)

Figure 1 and 2 shows the risk in form of a pictogram.

Figure 1.

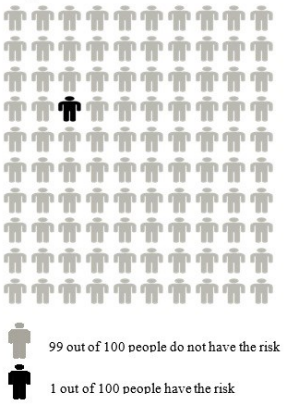
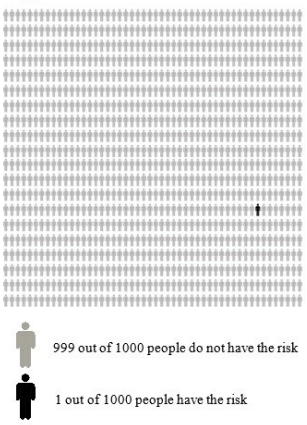


Figure 2



The collection of the swabs will not cause discomfort. Should your swabs test positive for bacteria resistant to common antibiotics, your treating team will be notified to ensure you receive any necessary review or treatment.

9 What will happen to my test samples?

This study involves the collection and storage of swabs. The swabs obtained for the purpose of this research project will be transferred to the Department of Infectious Diseases, Monash University.

The collection of the swabs, as described is an optional component of the research. The swabs will be stored to allow comparison of the isolated bacteria. The swabs will be individually re-identifiable (coded). Any identifiable data will be stored securely separately. It will only be disclosed with your permission. The swabs will be stored for 15 years in the Clinical Research Laboratory, Department of Infectious Diseases, Monash University and, after this time, will be discarded in the appropriate manner. The use of swabs for future research will be overseen by an appropriately constituted Hospital Research Ethics Committee. If you later choose to withdraw consent for future use of stored swabs, the Research Investigator will notify the Department of Infectious Diseases, housing the swabs and all your remaining swabs will be discarded in the appropriate manner and the disposition will be documented.

10 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form. Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

11 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

12 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

13 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:
• Unacceptable side effects
• The drug being shown not to be effective
• The drug being shown to work and not need further testing

14 What happens when the research project ends?

At the completion of this research project you will continue to be followed up by your treating doctors. We expect the project will be completed in December 2021. Once the results of the research are finalised all participants will be provided with a plain English summary of the findings upon request to the Clinical Trial Coordinator.

Part 2 How is the research project being conducted?

15 What will happen to information about me?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities, the institution relevant to this Participant Information Sheet, Epworth HealthCare or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

All data collected will be re-identifiable, however all data sent to the Study Project Office will be coded to maintain your privacy and confidentiality. Re-identifiable data will be stored either in folders (for paper records) or put into a secure computer, which can only be accessed by the researchers at this hospital. All written data will be stored for at least 15 years upon completion of the trial. Any data suitable for disposing, will be securely destroyed.

We plan to store the data in the secure study database indefinitely at the ASAP Trial Project Office. All DHS data supplied to researchers will be destroyed after 15 years.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

Information about your participation in this research project may be recorded in your health records.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

16 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

17 Who is organising and funding the research?

This research project is being conducted by Dr Trisha Peel and funded through a grant from the National Health and Medical Research Council of Australia (NHMRC). The Epworth HealthCare will receive a payment from the coordinating centre. This payment is to fund the salary of the research nurse undertaking this research project.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wage).

18 Who has reviewed the research project?

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 project have been approved by the HREC of The Alfred Hospital 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.

19 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on (03) 9936 8054 or any of the following people:

Clinical contact person

Name	Prof Richard de Steiger
Position	Epworth Victor Smorgon Chair of Surgery
Telephone	(03) 9936 8054
Email	Richard.desteiger@epworth.org.au

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

Complaints contact person

Name	Governance Officer
Position	As Above
Telephone	(03) 9936 8058
Email	research@epworth.org.au

If you have any complaints about any aspect of the project, 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	Alfred Hospital Ethics Committee
HREC Executive Officer	Research Governance Officer
Telephone	(03) 9076 3619
Email	research@alfred.org.au

Local HREC Office contact (Single Site - Research Governance Officer)

Name	Governance Officer
Position	*As Above*
Telephone	*(03) 9936 8058*
Email	*research@epworth.org.au*

Consent Form - *Adult providing own consent*

Title	Multicentre Randomised Double-Blind Placebo Controlled Trial of Combination Vancomycin and Cefazolin Surgical Antibiotic Prophylaxis
Short Title	Arthroplasty Surgical Antibiotic Prophylaxis (ASAP) Trial
Project Sponsor	Monash University
Co-ordinating Principal Investigator	Dr Trisha Peel
Principal Investigator	Prof Richard de Steiger
Location	Epworth HealthCare
HREC Number	HREC/18/ALFRED/102
Local Project Number	EH2018-358

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Epworth HealthCare concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

Staphylococcus Carriage Sub-Study

I consent to the collection, storage and use of skin swab samples taken from me for use, as described in the relevant section of the Participant Information Sheet, for:

- This specific research project
- Other research that is closely related to this research project
- Any future research.

Name of Participant (please print) _____

Signature _____ Date _____

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning the research project.

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation - *Adult providing own consent*

Title	Multicentre Randomised Double-Blind Placebo Controlled Trial of Combination Vancomycin and Cefazolin Surgical Antibiotic Prophylaxis
Short Title	Arthroplasty Surgical Antibiotic Prophylaxis (ASAP) Trial
Project Sponsor	Monash University
Co-ordinating Principal Investigator	Dr Trisha Peel
Principal Investigator	Prof Richard de Steiger
Location	Epworth HealthCare
HREC Number	HREC/18/ALFRED/102
Local Project Number	EH2018-358

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Epworth HealthCare.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.