OXFORD VACCINE GROUP

A Study Exploring Whooping Cough Protection in Children and Adults

Study Information Booklet

The Oxford Vaccine Group (OVG) is part of the University of Oxford and is an independent research team of doctors, nurses and play assistants. We carry out research studies of new and improved vaccines for babies, young children, teenagers and adults and teach doctors and nurses about immunisations. In the past 5 years alone, over 7000 participants in the Thames Valley area have taken part in our research studies.

You are invited to take part in a study looking at how well a vaccine for whooping cough (pertussis) works.

This study, which is being run by the Oxford Vaccine Group (OVG), is one of many projects that are part of the PERISCOPE Consortium, a group of scientists who have come together to research and improve understanding and knowledge of pertussis disease, as well as improve future development of pertussis vaccines.

Before you decide whether to take part, it is important for you to understand what the study is about and what participation would involve. Please take time to read the information carefully, and discuss with others if you wish. If anything is unclear or you would like further information, please contact the study team.

Thank you for taking the time to consider taking part in the study.

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Summary

This booklet is directed to the adults that might participate in this study

- We are researching pertussis (whooping cough) which is a highly infectious respiratory (lung) illness with severe complications in infants. In recent years, there has been an increase in the number of cases despite good vaccination coverage
- **What do we want to do?** We want to understand how the immune system, which protects us against infections, responds after the administration of a whooping cough vaccine in different age groups
- **How are we going to do it?** OVG will recruit 36 children and 25 adults for each age group (A: 7-10 years; B: 11-15 years; C: 20-34 years and D: 60-70 years). During the study they would receive a whooping cough vaccine and we would need to take a small amount of blood at different times
- The study is also taking place in the Netherlands and Finland. The vaccine and blood sampling will be done in the consulting rooms of the Centre for Clinical Vaccinology and Tropical Medicine (CCVTM) at the Churchill Hospital site
- 24-hour contact to a study doctor is going to be available during the study
- We would reimburse you £45 per visit
- Please note, your GP must be within the Thames Valley Area in order to be able to participate in this study.

Why have I been invited to take part?

You have been approached because you were born in a year that means you are likely to have been vaccinated against whooping cough and are within the age range that we are targeting for our study. You also live within an area where the study is being carried out. Taking part in this study is **voluntary**.

What is pertussis disease and whooping cough?

Pertussis, most commonly known as 'whooping cough', is caused by the bacterium called *Bordetella pertussis*. It is a highly infectious respiratory infection that affects the airways and the lungs. In infants, particularly in those that have not received the pertussis vaccine, the disease can lead to severe complications such as pneumonia,

difficulty with breathing and seizures. Some infants require hospital admission and sometimes need a ventilator to help with breathing. In some of these cases, pertussis can result in death.

Whooping cough normally presents with symptoms such as a runny nose and cough that can last for 1-2 weeks. Some pertussis disease can become more serious after this time, causing severe, persistent coughing, which can cause vomiting, and again difficulty in breathing. These symptoms can last for 2-3 months. The droplets produced from the coughing allows the infection to spread easily from person to person. Some individuals can carry the bacterium without any symptoms, but they can still spread it to others.

Not only children are affected by whooping cough. In high-income countries like the UK, the number of cases in older children and the elderly are increasing, with increased risk of spreading the disease to the most vulnerable groups. In these groups symptoms such as coughing are more prolonged and can cause problems with sleep, loss of time for school/work or other activities.

What are we interested in?

In this study, we are interested in learning more about a vaccine that protects against whooping cough. **Vaccines** stimulate our immune system to make antibodies, which move around the body in the blood to protect us against infections. If a child or an adult comes into contact with an infectious disease against which they have been vaccinated (or "immunised"), their body will be able to recognise and fight the disease. This is known as an **immune response.** Without vaccines, people are at increased risk of catching many serious diseases.

There are two different types of pertussis vaccine available worldwide, 'acellular' and 'whole cell'. The whole cell vaccine was the first pertussis vaccine to be available in the world and was introduced into the UK routine schedule in 1957.

The UK switched from using the whole cell vaccine to the acellular vaccine in 2004. The main reason for this change was that the whole cell vaccine was known to cause more reactions (such as fever, redness and swelling at the site of the injection) when compared with the acellular vaccine.

In the past few years, the number of cases of pertussis has increased in countries like the UK despite good vaccine coverage. In 2012, the number of pertussis cases rose significantly, causing 14 deaths in England and Wales all in children under 3 months of age. Several countries around the world have also been affected, including European countries, Australia and the US, all with high vaccination coverage. There have been suggestions by researchers, but no definitive answers, as to why this may be happening (for example, the acellular vaccine may not give such long-term protection, or there may be an increase in circulation of the bacterium). For both these reasons, researchers are questioning whether the introduction of the acellular vaccine, replacing the whole cell vaccine in high-income countries, has contributed to this increase. We hope that the information we get from this study will help us to understand this.

In this study, we want to understand the immune response after the administration of a dose of acellular pertussis vaccine in different age's groups (7-10 years, 11-15 years old, 20-34 years old and 60-70 years old). The reason to have different age groups is that depending on your age a different vaccination schedule was available in the UK. We expect that younger children will have been only vaccinated with acellular vaccine, older teenagers and young adults with only acellular or a mixed of both vaccines and older people with only whole cell vaccine.

The use of different age groups allows us to understand the differences in immune responses and the differences in the duration of that immunity considering those different schedules. Currently we still don't know how long the vaccine protection can last, but we know that immunity is lost as the years pass by. This study intends to help answer that question.

What happens in the study?

This study will also be conducted in other countries such as the Netherlands and Finland. OVG will enrol 36 children and 25 adults for each age group (A: 7-10 years old; B: 11-15 years old; C: 20-34 years old and D: 60-70 years old) from the Thames Valley. We are specifically looking to enrol you if you are either aged **20-34 years old**, or **60-70 years old.**

All adults enrolled in the study at the time of the first visit would receive a vaccine called Boostrix®-IPV that protects against whooping cough, diphtheria, tetanus and poliomyelitis. The vaccine will be administered intramuscularly in the arm. On the same visit a blood sample will be taken. Another four blood samples at different time points will be taken as shown in table 1. If the study team is unable to obtain a blood sample from you, you may be given the option to re-schedule the appointment, dependent on the timelines allowed for that visit or miss that sample. You will be followed-up by the study team until 1 year after the first visit. A total of 5 visits will be performed. Please read the table in detail, as we will need you available to be seen at **all** 5 visits.

Timeline/ Visit	T0 Day 0 First visit	T2 Day 7	T3 Day 14	T4 Day 28	T5 Day 365
Study Procedures					

Table 1: Study visits and activities performed in each visit

The first appointment should last around an hour and all following appointments about 30 minutes. You would also have 24hr telephone access to a study doctor should you have concerns relating to the study. We would also let your GP know that you are taking part in the study.

What are the risks/possible side effects of the vaccines and of blood sampling?

Blood sampling

The blood sampling may be uncomfortable but it will be performed by trained staff. There may be some short lived bleeding and/or bruising following the blood sample. Some people also experience dizzy spells or fainting. A maximum of 40ml of blood would be obtained at each visit. For the duration of the study, this would total a

maximum of 180ml, which is less than 1 “blood donation” to the UK Blood Transfusion Service. Your body would replace this blood quickly.

Vaccines

The vaccine that is going to be administered in this study (Boostrix®-IPV) is similar to other whooping cough vaccines already administered in the standard immunisation programme. The Boostrix®-IPV vaccine is a licensed vaccine, meaning that it has met the rigorous safety standards required by European regulators.

The side effects after vaccination could be divided into local or general and both are normally mild to moderate and short lived. The most common side effects with this vaccine are the local side effects including some redness and mild swelling where the injection is given in your arm. Other general side effects include irritability, sleepiness, and loss of appetite, headache and fever.

Some people have reported allergic reactions (sometimes severe). An immediate severe allergic reaction (anaphylaxis) can result in a rash, swelling of the body and breathing difficulties. The study team would observe you for 15 minutes following the vaccination as this is the time most reactions are expected to happen. The study team members carry adrenaline (medicine to treat anaphylactic reactions) and are trained to administer it should such a reaction occur.

Do I have to take part?

No. We are looking for volunteers. Should you volunteer and later change your mind (for whatever reason) it is your right to do so, and you would not need to provide an explanation to the study team or anyone else.

If you did take part, you are also free to change your mind and withdraw at any time without giving an explanation. If you did withdraw we would use the samples and data we have collected from you in our analysis up until the point you informed us that you wanted to withdraw. If consent was obtained for storing samples beyond the end of the study period, we will ask if you wish to withdraw from this also. We would not collect any further samples, but we may ask you to allow us to phone you or have you visit the study centre (e.g. for a follow-up visit to check for any side effect you may have had during your time on the study) after you withdrew. Whatever you choose it

is important that you are happy with your decision and it is not the role of the study team to help decide for you. We would help present the details of the study and answer all your questions so you could make an informed decision.

What are the possible benefits of taking part?

As part of the study, you will receive a vaccine that will provide protection against whooping cough, diphtheria, tetanus and poliomyelitis. The information gained from this study will also help to develop methods that can be used to understand and improve whooping cough vaccines in the future.

Is there any reimbursement for the time spent during the participation in the study?

All adult participants are reimbursed for their time, travel and the inconvenience of blood samples, and would receive £45 per visit. Participants will receive a maximum of £225 if they remain in the study for the entire period and attend all study visits. Payments will be made via bank transfer. Participants will be asked to provide banking details including account name, sort code, account number and national insurance number. All details will be stored confidentially and retained by the Oxford Vaccine Group while the participant is actively involved in the study.

Participant payments will be requested after the completion of the first four visits and then again after the final visit. If you choose to leave the study early or are withdrawn from the study, you would be reimbursed according to the length of your participation based on these figures.

What to do if I wish to take part?

If you are interested in taking part, please respond by returning the reply slip included with this booklet or alternatively email/phone the Oxford Vaccine Group and a member of the study team would discuss the study with you in more detail via the telephone. We would then arrange an appointment to see you at your convenience to answer any further questions that you may have. If you are then keen to proceed and comfortable with your decision then we would ask you to sign an **informed consent form**. Only once this is signed would we then start any study procedures. Study visits would be conducted in the consulting rooms of the Centre for Clinical

Vaccinology and Tropical Medicine (CCVTM) at the Churchill Hospital site. You will also have 24hr telephone access to a study doctor should you have concerns relating to the study.

For females only:

Although the study vaccine (Boostrix®-IPV) is recommended routinely from 16 weeks gestation in pregnancy and has been used routinely in pregnant women and therefore considered safe, pregnancy is an exclusion criteria for studies conducted at the Oxford Vaccine group. Therefore, please be aware that for cohort C (20-34yr olds, where the probability of childbearing is higher), a urine pregnancy test would be performed prior to any vaccination, that is, on the day of vaccination (T0).

What will happen to any of my samples?

The samples we take for this study will be labelled with a study number and tested anonymously in certified laboratories.

If you choose to take part in this study, you will need to agree to the PERISCOPE consortium storing components of your blood, including DNA, in a collection of samples within the PERISCOPE Biobank (located at the Radboud University Medical Centre, Nijmegen, the Netherlands.), for the duration of the study. Samples from the Biobank will only be used for the study purposes and objectives of the PERISCOPE project. The material given to researchers will not have information that identifies you. However, your DNA is unique to you so it can never be completely anonymous.

The PERISCOPE biobank also includes storage of left over samples at the end of this project. Samples that are left over will only be used to answer the research questions of the PERISCOPE project, but may be shared with hospitals, universities, non-profit institutions or commercial laboratories worldwide. The storage and use of **left over** samples is voluntary. If you do not consent to the further use of your samples, they will be destroyed immediately following the completion of this study.

What happens when the study stops?

Once all participants within the study have completed their relevant visits, we will start the analysis and interpretation of the findings. Once complete, a publication will

be written and published. Following this, we will notify you of the results and provide a link to the published paper. This whole process can take anywhere from one to three years after completion of all study visits for all participants. Any publications arising from our studies are listed on the Oxford Vaccine Group website.

Will my participation in the study be kept confidential?

The Oxford Vaccine Group (OVG) alone would hold any study records with your name and address. Your participation in the study would remain confidential and when the results of the study were published, you would not be identified. If you decided to take part in the study, we would inform your GP practice that you are enrolled in the study. To ensure that all personal information is kept confidential you would be allocated a study number. This would be used to identify you on any paperwork or samples taken. You would not be identifiable to laboratory staff handling study samples.

Information kept by the OVG would include your demographic details, medical history and results of blood sample analysis. To check that the study was being conducted correctly, your study records might be read (but not kept) by representatives of the following groups who are obliged to treat your information confidentially:

- UK Medicines and Healthcare products Regulatory Agency (MHRA)
- The NHS trusts that have given approval for this study
- Responsible members of the University of Oxford may be given access to data for monitoring and/or audit of the study to ensure we are complying with regulations.

We would also seek your consent to register your name on 'The Over-volunteering Prevention System' (TOPS) national database. This is designed to guard against the potential for harm that can result from excessive clinical trials involving investigational products and blood donations. This would be done using your National Insurance number, or passport number, and all information would be kept confidential.

Your study information, removed of any identifying information, may be sent outside of the European Union, including to commercial partners. By signing the consent form for this study, you would be giving permission for this. Any information that identified you would remain with the OVG.

Your Data

We will be using information collected from you and your medical records in order to undertake this study. Research is a task that we perform in the public interest. The University of Oxford, as sponsor, is the data controller. This means that we, as University of Oxford researchers, are responsible for looking after your information and using it properly. We will use the minimum personally-identifiable information possible. We will keep identifiable information about you for the time period of 10 years after the last participant has completed the study or until the youngest participant has reached 21 years of age after the end of the study. We will store the anonymised research data and any research documents with personal information, such as consent forms, securely at the University of Oxford for a period of 10 years after the last participant has completed the study or until the youngest participant has reached 21 years of age after the end of the study. This will be reviewed every 5 years and files will be confidentially destroyed if no longer needed. Electronic data will be stored securely for the same time in the University of Oxford electronic archives

What else do I need to know?

The vaccine used in this study (Boostrix®-IPV) is a licensed vaccine in Europe, including the UK. We do not anticipate any harm resulting from obtaining blood samples. The University of Oxford, as UK Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study.

What will happen to the results of the research study?

We plan to publish the results in a medical journal that will be accessible to the public. None of the reports will contain any information that might allow the readers to identify anyone who took part in the study. At the end of the study, we will also write to all participants to summarise the overall findings.

Who is organising and funding the research?

The study is funded by the Innovative Medicines Initiative (IMI), who are funded jointly by the European Union and the Bill and Melinda Gates Foundation (represented by the European Commission) as well as the European pharmaceutical industry (represented by EFPIA, the European Federation of Pharmaceutical Industries and Associations)., The study is also being co-sponsored by University of Oxford, Rijksinstituut voor Volksgezondheid en Milieu National Institute for Public Health and the Environment – RIVM (The Netherlands) and Turun Yliopisto (Turku University) (Finland).

Who reviewed the study?

An independent group of people called a Research Ethics Committee looks at all research in the NHS, to protect the safety, rights, well-being and dignity of individuals. This study has been reviewed and given favourable opinion by the East Midlands – Nottingham 2 Research Ethics Committee (Ref: 18/EM/0022). Details of this study can be found on the following website: www.clinicaltrialsregister.eu (Ref: 2016-003678-42).

What if I wish to complain?

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the Oxford Vaccine Group on 01865 611400 or email info@ovg.ox.ac.uk. You can also contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480 or email ctrg@admin.ox.ac.uk

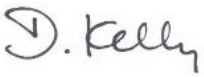
What do I do now?

You do not need to make a final decision straight away. Please contact us by:

- **E-mail: info@ovg.ox.ac.uk**
- **Telephone: 01865 611400**
- **Website: www.bertstudy.com**

Members of the research team will be happy to discuss the study with you and answer any questions you may have.

Yours sincerely,



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