OXFORD VACCINE GROUP

A Study Exploring Whooping Cough Protection in Children and Adults

Parent 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.

Your child is invited to take part in a study looking at how well vaccines for whooping cough (pertussis) work. Everything that we need to do for the study would be done at your home. 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 you would like your child to take part, it is important for you and them 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.

Contents

Summary

This booklet is directed towards parents of children that are invited to 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 giving a whooping cough vaccine to people in different age groups.
- **How we are 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 will receive a whooping cough vaccine and we will 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 would be performed at your home or in a location near you (if this is in a clinic, you would be reimbursed for car parking charges).
- A doctor will be available for phone contact, 24 hours a day during the study period.
- Please note, your child's GP must be within the Thames Valley Area in

Why has my child been invited to take part?

You have been approached because your child was born in a year that means s/he is likely to have been vaccinated against whooping cough. S/he is also at the age that we are targeting for our study, and you live in 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 that 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.

Children are not the only ones 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 vaccines 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 giving a dose of acellular pertussis vaccine in different age groups (7-10 years old, 11-15 years old, 20-34 years old and 60-70 years old). The reason for having different age groups is that depending on your child's age a different type of pertussis vaccine was available in the UK. We expect that younger children will have been vaccinated only with acellular vaccine, older teenagers and young adults with only acellular or a mixture of both vaccines, and older people only with whole cell vaccine. The use of different age groups will allow us to understand differences in immune responses and differences in how long immunity lasts in people who have followed different pertussis vaccination schedules. Currently there are still a lot of questions about how long vaccine protection can last, although we do know that immunity is lost as the years pass by. This study will help to answer these questions.

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.

If you agree your child can take part, a member of the study team will arrange an appointment to meet you at your home or at a location near you, to answer any further questions that you may have, check the health of your child and complete the consent form. Your child will also be given information about the study for them to read (this can be with you if they are young) and we will answer any questions they might have. Children aged **11-15yrs** will be asked to sign a form if they agree to take part. Children aged **7-10yrs** will not sign a form but will still have to agree before we continue. In all age groups, a consent form will need to be signed by a parent.

The children in each age group (A: 7-10 years old; B: 11-15 years old) will be divided into sub-groups in order by which they are enrolled onto the study, whilst taking into account individual availability. The only difference between the subgroups is the time when the blood samples are taken.

All children enrolled in the study at the time of the first visit will receive a vaccine called Boostrix®-IPV that protects against pertussis, diphtheria, tetanus and polio. Your child will have received a similar vaccine when they were younger. The vaccine will be injected into the arm muscle. At the same visit, a blood sample will be taken. Another three blood samplings at different time points will be carried out as shown in table 1 and 2. The blood samples will allow us to measure the antibodies and other immune responses that your child has made in response to the vaccine. Between 14 and 26 mls (3-5 teaspoons) will be taken at each visit. A maximum of 62mls (approximately 12 teaspoons) for ages 7-10 and a maximum of 102mls (approximately 20 teaspoons) for ages 11-15 will be taken over the one-year study period. In order to minimise any distress caused by the blood test procedure, a local anaesthetic cream is used to numb the skin before taking the blood sample (provided to you prior to the visits with explanation of use). EMLA® will be the first anaesthetic cream to be supplied, but this can be replaced by AMETOP® in case of a previous or new allergy to EMLA®.We would only have a maximum of 2 attempts at obtaining the blood (parent and child would have a final decision to proceed with 2nd attempt if the 1st one is not successful). If the

study team is unable to obtain a blood sample from your child, you and your child may be given the option to re-schedule the appointment, (dependant on the timelines allowed for that visit), or miss that sample.

The study team will follow up your child until 1 year after the first visit. A total of 4 visits will be performed, in your house or in a location near you.

	Timeline/ visit	T0 (Day 0)	T2 (Day 7)	T3 (Day 14)	T4 (Day 28)	T5 (Day 365)
Age 7-10 Year olds	Subgroup					
	1					
	2					

Table 1: Study visits and procedures performed in each visit and subgroup

	Timeline/ visit	T0 (Day 0)	T1 (Day 1)	T2 (Day 7)	T3 (Day 14)	T4 (Day 28)	T5 (Day 365)
Age 11-15 Year olds	Subgroup						
	1						
	2						
	3						

Table 2: Study visits and procedures performed in each visit and subgroup

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

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

Blood sampling

The blood samples may be uncomfortable but it will be performed by trained staff and anaesthetic cream will be provided to minimise discomfort. There may be some short-lived bleeding and/or bruising following the blood sampling. Some people also experience dizzy spells or fainting.

Vaccines

During this study, the vaccine we are using (Boostrix®-IPV) is similar to other pertussis vaccines given to your child previously. The side effects after vaccination can be divided into local or general side effects and both are normally mild to moderate and short lived. The most common side effects with this vaccine are some redness and mild swelling where the injection is given. Other general side effects are irritability, sleepiness, 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 your child 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.

Does my child have to take part?

No. Taking part in this research study is voluntary and if you or your child decide to say no, it will not affect your child's routine care in any way. If your child did take part, you or they are also free to change your/their mind and withdraw your child at any time without giving an explanation. If you did withdraw your child from the study and a blood sample/s has already been taken, we would use the sample/s and data we have collected from your child in our analysis up until the point you informed us that you wanted to withdraw. If consent was obtained for storing samples for future research 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 arrange a visit for a follow-up visit to check for any side effect your child may have had during their time on the study after withdrawal.

Whatever you choose it is important that you and your child are happy with the 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?

Your child would benefit from taking part in this study by receiving a vaccine that is not currently given to children this age and will increase protection against pertussis, diphtheria, tetanus and polio. The vaccine will also be administered at your home. There is also a benefit to the community, as our results will be used to decide future vaccination policy in the UK and Europe.

Children in year 9 routinely receive Td-IPV (Revaxis®) and MenACWY vaccine (Nimenrix® or Menveo®) as part of their school leavers vaccines. Some children will still be a part of the study when they are offered the school leavers booster. For these children their study dose of dTaP-IPV (Boostrix®-IPV) will have been sufficient and the school leaver Td-IPV (Revaxis®) booster is not needed. They will still need the MenACWY vaccine (Nimenrix® or Menveo®). For younger children who have already completed the study before they are offered the school leavers vaccines they would need to receive both Td-IPV (Revaxis®) and MenACWY vaccine (Nimenrix® or Menveo®) as part of their school leavers vaccines.

If your child may wish to take part

If you and your child were 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 will discuss the study with you in more detail via the telephone. We would then arrange an appointment to meet you and your child at your home, to answer any further questions, check their health and complete the consent form if you wish to proceed with the study.

You will also find enclosed with this booklet, an age appropriate information booklet for your child. We advise your child to read it carefully, because we consider that his/her opinion about participating in the study is very important. That information will be discussed with you and your child within the first visit and we will only go ahead with the study if you and your child are happy to participate and s/he understands what will happen. The first appointment should last around one and a half hours and all following appointments around 30 minutes.
You will also have 24hr telephone access to a study doctor should you have concerns relating to the study. We will let your GP, health visitor and child health department know that your child is taking part in the study.

For female children only:
Although this vaccine is considered safe in pregnancy and given routinely in the UK immunisation schedule to pregnant woman, pregnancy is an exclusion criteria for studies conducted at the Oxford Vaccine Group, therefore please be aware that if your child has had their first period, the doctor or nurse **will ask** if there is a possibility she may be pregnant before giving her the vaccine. Should it be appropriate as the parent/guardian you will be present during this conversation. If there is a possibility your daughter is pregnant, she would not be able to have the vaccine or continue in the study and we would need to inform her GP.

What will happen to any samples from my child?

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 and your child will need to agree to the PERISCOPE consortium storing components of your child's 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 your child. However, DNA is unique so it can never be completely anonymous.

The PERISCOPE biobank also includes the storage of left over samples following the end of the 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 child's samples, they will be destroyed immediately following the completion of this study.

What happens when the study stops?

Once all children and adults 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. All publications from our studies are listed on the Oxford Vaccine Group website.

Will my child's participation in the study be kept confidential?

The Oxford Vaccine Group (OVG) alone would hold any study records with your child's name and address. Your child's participation in the study would remain confidential and when the results of the study were published, your child would not be identified. If you and your child decided to take part in the study, we would inform your GP practice that your child is enrolled in the study and of the dates that we gave your child his/her study vaccine.

To ensure that all personal information is kept confidential your child would be allocated a study number. This would be used to identify your child on any paperwork or samples taken. Your child would not be identifiable to laboratory staff handling study samples.

Information kept by the OVG would include your child's demographic details (such as name, address and date of birth), medical history and results of blood sample analysis. To check that the study was being conducted correctly, your child's 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.

You and your child's 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 your child 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 child's information and using it properly. We will use the minimum personally-identifiable information possible. We will keep identifiable information about your child 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.clinicaltrials.gov (Ref: NCT03697798).

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

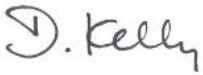
Vaccine Group on 01865 611400 or email info@ovg.ox.ac.uk. You can also contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480 or email ctrg@admin.ox.ac.uk

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**

Yours sincerely,



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