Who Sponsored this study?
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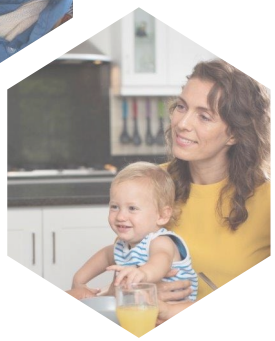
A STUDY TO FIND OUT IF THE COMBINED DIPHTHERIA, TETANUS AND WHOOPING COUGH VACCINE GIVEN TO PREGNANT WOMEN CAN ALSO HELP TO PROTECT THEIR BABIES



GSK would like to thank all the pregnant women who took part in this clinical study. We think it is important that you know the study results. We hope it helps you understand and feel proud about your important role in medical research.

Overview

Why was this study conducted?

The main goal of this study was to see if a combined diphtheria, tetanus, and whooping cough vaccine (Tdap vaccine) when given to pregnant women can help to protect their babies.

What was studied?

The study looked at,

- Body's defenses (called antibodies) in pregnant women and in newborns.
- Safety of vaccinating pregnant women (for both mother and baby).

Who was in this study?

687 healthy pregnant women 18 to 45 years old. The study was done in Australia, Canada, Czechia, Finland, Italy and Spain.

What kind of study was it?

- Randomized: pregnant women were assigned by chance to receive either the Tdap vaccine or a placebo.
- Observer-blinded: neither the study doctors nor the pregnant women knew if they received the vaccine or the placebo.
- Phase IV study: the Tdap vaccine is available in the market.

Main results

- Pregnant mothers who got the Tdap vaccine passed more antibodies against whooping cough to their babies than those who got placebo.
- Results suggest that the Tdap vaccine was safe both for mothers and their babies.

NCT number: NCT02377349
EudraCT number: 2014-001119-38

General information about the research study

When was the study done?

The study started on 14-October-2015 and ended on 24-October-2017.

Why was this study done?

Whooping cough is caused by bacteria. It is named after the "whoop" sound that infected people make when coughing. It spreads easily from one person to the other. If it is not treated, this disease can be serious and may lead to death especially in babies.

As the vaccine does not work in young babies, one possibility to protect those babies is to give the mother a vaccine during pregnancy. The mother's body defenses (called **antibodies**) can pass to the baby before birth offering some protection until the baby is old enough to receive the vaccine.

GSK makes a combined vaccine against whooping cough, diphtheria and tetanus (called Tdap vaccine).

The main goal of the study was to see:

- If pregnant mothers who got the Tdap vaccine passed more antibodies against whooping cough to their newborns than pregnant women who received placebo.

Additionally, the study also wanted to look at:

- The safety of vaccinating pregnant women (for both mother and baby).
- The presence of antibodies against whooping cough in pregnant women and in the blood from the umbilical cord (called "cord blood").
- The percentage of pregnant women with protective levels of antibodies against diphtheria and tetanus.

Additional measurements were done as well. All results of this study can be found in the ***clinical results summary.***

Who took part in this study?

687 pregnant women from 6 countries took part in the study:

Women could take part in the study if they:

- ✓ Were in good health.
- ✓ Were 18 to 45 years old
- ✓ Were 27 to 36 weeks pregnant when they started the study

Women could not take part in the study if they:

- x Were at risk of complications of pregnancy
- x Planned to give their baby up for adoption or place the baby in care

Which vaccines were studied?

- **Tdap vaccine**: a combination vaccine that is used to protect against three infectious diseases: diphtheria, tetanus and whooping cough.
- **Placebo**: a saline water solution.

How was the study done?

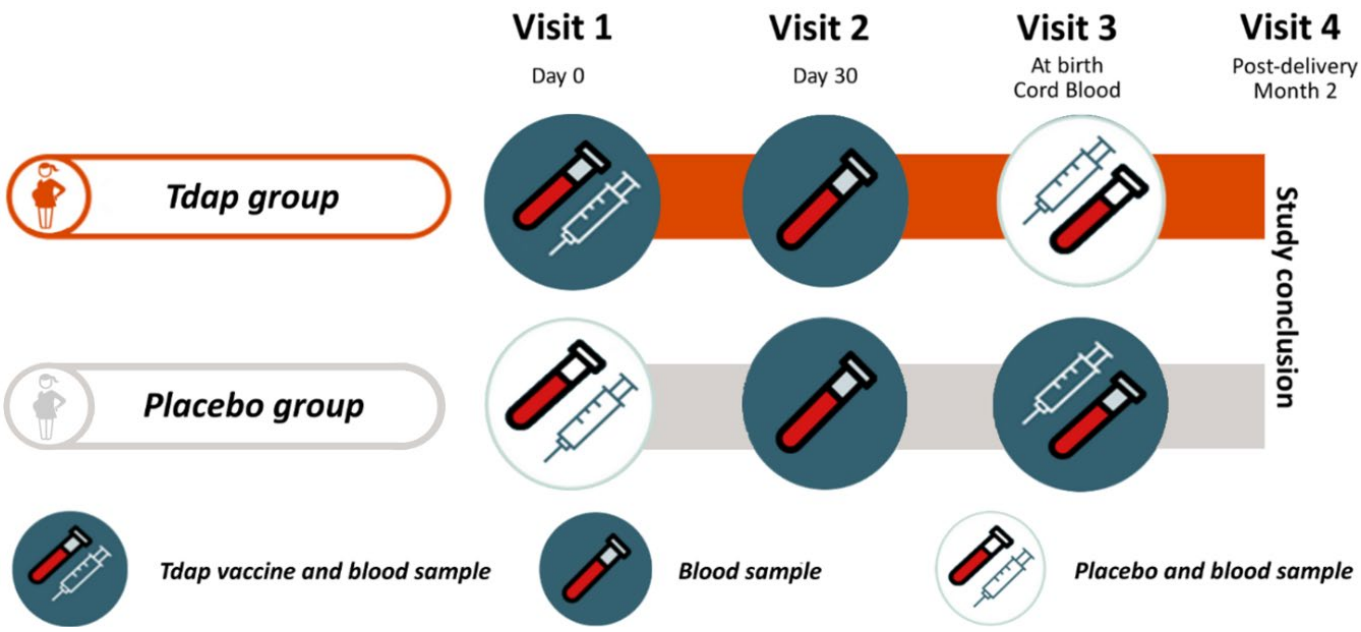
The pregnant women were placed in 2 study groups:

- **Tdap group**: In this group, women got the *Tdap vaccine* during pregnancy and a *placebo* soon after delivery.
- **Placebo group**: In this group, women got the *placebo* during pregnancy and a *Tdap vaccine* soon after delivery.

Blood samples were taken before and after the injection of the vaccine or placebo during pregnancy. Blood from the umbilical cord (called "**cord blood**") was collected after birth. The blood samples were then tested to compare the amounts of antibodies in the 2 groups.

The study took about 5 months for each mother.

Figure 1. Study design - Overview of time and events



What were the main results of the study?

This report focuses only on the results of the main goals of the study. All results may be found in the clinical results summary.

The main goal of the study was to look at the amounts of antibodies that were transferred from the mothers to their babies through the umbilical cord. The results are presented in Figure 2.

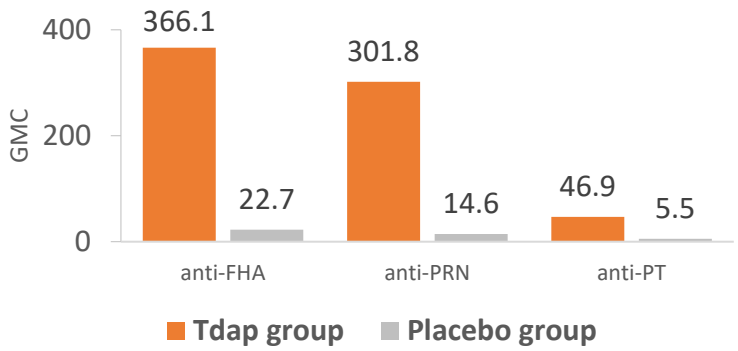
Measuring antibody levels against whooping cough, diphtheria and tetanus in pregnant women were additional goals of the study. The results are presented in Figure 3 and Figure 4.

Antibodies against whooping cough in pregnant women and newborns

Researchers measured 3 types of antibodies against whooping cough (called 'anti-FHA', 'anti-PRN' and 'anti-PT') in the cord blood.

The pregnant women who got the Tdap vaccine passed more antibodies against whooping cough to their babies than those pregnant women who got the placebo (Figure 2).

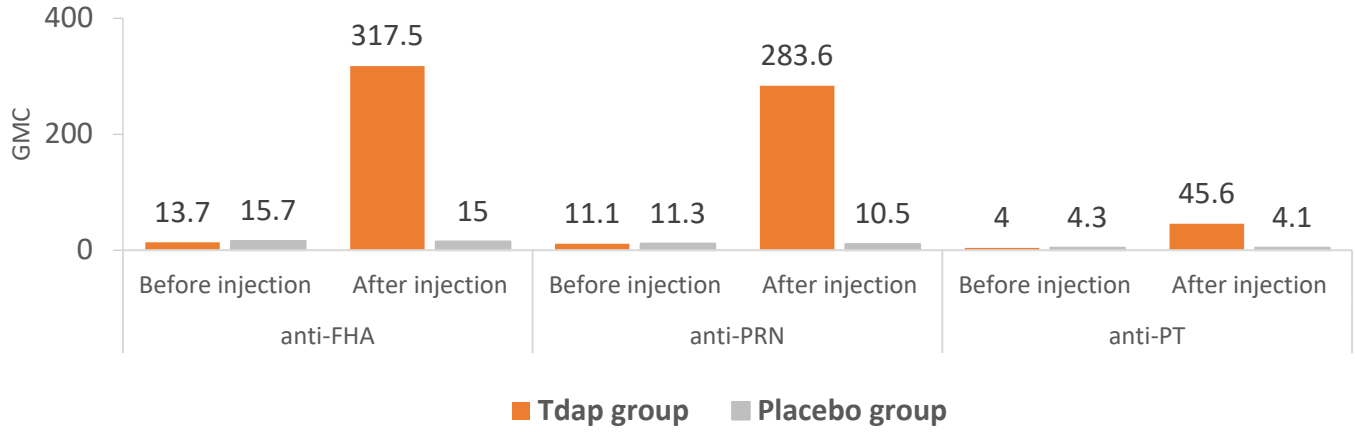
Figure 2. Average amounts of antibodies against whooping cough in cord blood.



Geometric Mean Concentration (GMC) is a measure of the average amount of antibodies in blood.

The same 3 types of whooping cough antibodies were measured in the pregnant women (Figure 3). The amounts of antibodies were 11 to 25 times higher after vaccination than before in the Tdap group. In the placebo group, the amounts of whooping cough antibodies did not change.

Figure 3. Average amounts of antibodies against whooping cough in pregnant women.



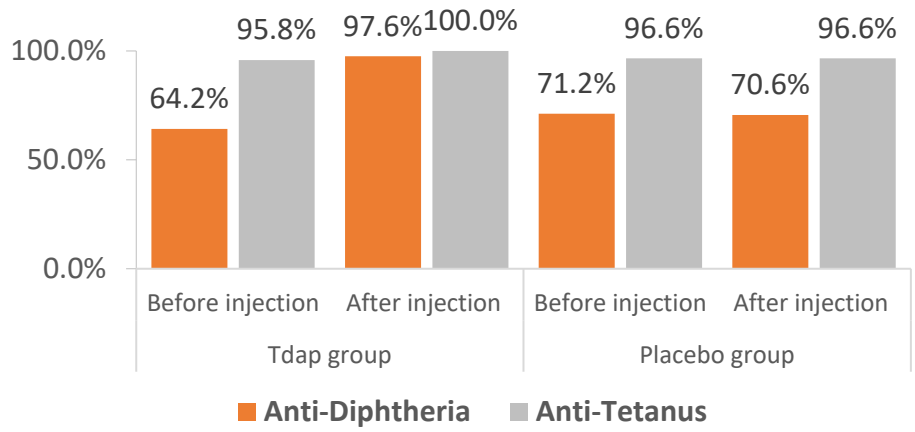
Geometric Mean Concentration (GMC) is a measure of the average amount of antibodies in blood.

Antibodies against diphtheria and tetanus in pregnant women

For diphtheria and tetanus, it is known that people are protected against the disease if the amount of antibodies in their blood is above a certain level. This is called the protective antibody level.

One month after the injection, almost all women in the Tdap group had protective antibody levels against diphtheria and tetanus. In the placebo group, 70.6% had protective antibody levels against diphtheria. Against tetanus this was 96.6% (Figure 4).

Figure 4. Percentages of pregnant women with protective antibody levels against diphtheria and tetanus



Pregnancy outcomes

Researchers also looked at specific unwanted medical events (adverse events) during pregnancy and in the newborns.

Figure 5, below, shows the number of birth defects reported during the study. The numbers were similar in both study groups.

These results suggest that the Tdap vaccine was safe both for mothers and their babies. All the results can be found in the ***clinical results summary***.

Figure 5. Pregnancy outcomes in both study groups

	Tdap group	Placebo group
Baby born with no birth defects	97.4% (332/341)	97.4% (337/346)
Baby born with birth defects	2.6% (9/341)	2.3% (8/346)

What were the side effects?

Unwanted medical events (adverse events) can happen to people when they receive a vaccine. Study doctors record all these events. A summary of all events reported in this study may be found in the clinical results summary.

If the study doctor thinks that the event was caused by the vaccine, they record this as a possible side effect (adverse reaction).

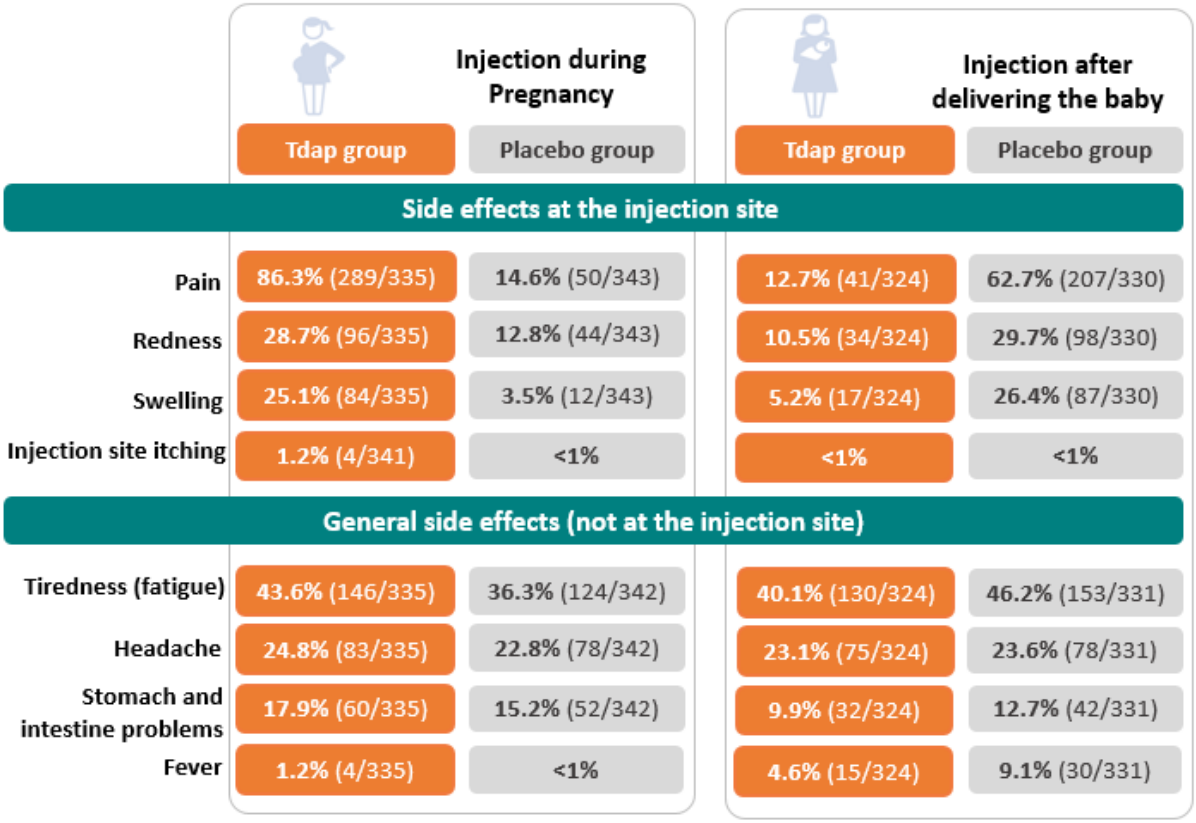
In this summary, "side effects*" refer to those events that the study doctor thinks may have been caused by the study vaccine.

The figure below shows the side effects at the injection site and other side effects reported by more than 1% of the women in any of the two groups.

** The use of the term side effects in this summary may be different to that in the Informed Consent or other documents related to the vaccine.*

The most common side effect at the site of injection was pain and the most common general side effect was tiredness (Figure 6).

Figure 6. Side effects reported by more than 1% of the women



	Injection during Pregnancy		Injection after delivering the baby	
	Tdap group	Placebo group	Tdap group	Placebo group
Side effects at the injection site				
Pain	86.3% (289/335)	14.6% (50/343)	12.7% (41/324)	62.7% (207/330)
Redness	28.7% (96/335)	12.8% (44/343)	10.5% (34/324)	29.7% (98/330)
Swelling	25.1% (84/335)	3.5% (12/343)	5.2% (17/324)	26.4% (87/330)
Injection site itching	1.2% (4/341)	<1%	<1%	<1%
General side effects (not at the injection site)				
Tiredness (fatigue)	43.6% (146/335)	36.3% (124/342)	40.1% (130/324)	46.2% (153/331)
Headache	24.8% (83/335)	22.8% (78/342)	23.1% (75/324)	23.6% (78/331)
Stomach and intestine problems	17.9% (60/335)	15.2% (52/342)	9.9% (32/324)	12.7% (42/331)
Fever	1.2% (4/335)	<1%	4.6% (15/324)	9.1% (30/331)

How has this study helped patients and researchers?

This study helped patients and researchers to know more about the Tdap vaccine when given to pregnant women and increased knowledge about maternal immunization against whooping cough, diphtheria and tetanus.

Are there plans for further studies?

Parents of babies born in this study will be invited to enroll those babies in two further studies. Babies in these studies will be given a primary and booster vaccination.

Where can I find more information about this study?

The detailed title for this research study is:
A Phase IV, observer-blind, randomized, cross-over, placebo-controlled, multicentre study to assess the immunogenicity and safety of a single dose of *Boostrix* in pregnant women.

Clinical studies have unique study numbers. Below are the unique study numbers associated with this study.

Organization	Website	Study Number
European Medicines Agency	www.clinicaltrialsregister.eu	2014-001119-38
United States National Institutes of Health (NIH)	www.clinicaltrials.gov	NCT02377349

Your doctor can help you understand more about this study and the results. You should not make changes to your care based on the results of this or any single study.

This document provides a short summary of this study for a general audience. You can find more information in scientific summaries of the study. Links to those summaries are provided at the end of this document.

This document was developed and approved by GSK on <<22-FEB-2019>>. The information in this summary does not include additional information available after this date.

For readers of this document in text form, the websites associated with the hyperlinks above are:

EudraCT summary:
https://www.clinicaltrialsregister.eu/ctr-search/search?query=2014-001119-38

US NIH/clinicaltrials.gov:
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