Subject information for participation in medical research

Human papillomavirus (HPV) vaccine effectiveness study among men who have sex with men (HPV4M)

Official title (in Dutch): Onderzoek naar effectiviteit van humaan papillomavirus (HPV) vaccin onder mannen die seks hebben met mannen

Introduction

Dear Sir,

With this letter, we would like to ask you to take part in a medical study. Participation is voluntary. You have received this letter because you are invited for the human papillomavirus (HPV) vaccination catch-up programme for people 19 years and older. We would like to measure how often HPV infections are found in men who have sex with men (MSM) born between 1996 and 2003. We do this by measuring how many HPV infections they have before vaccination and how many HPV infections they have two years after vaccination. Furthermore, we compare MSM who received the HPV vaccination with MSM who did not receive the HPV vaccination. You can read about the medical study in this information sheet, what it means for you, and what the pros and cons are. It is a lot of information. Can you please read the information and decide if you want to take part? If you want to take part, complete the form in Appendix D.

Ask your questions

You can take your decision based on the information in this information sheet. We also suggest that you do this:

- Put your questions to the investigator who gave you this information.
- Talk to your partner, family or friends about this study.
- Ask questions to the independent expert. For contact details, go to appendix A.
- Read the information on www.rijksoverheid.nl/mensenonderzoek.

1. General information

The Public Health Service (GGD) of Amsterdam has set up this study. Below, we always call the Public Health Service (GGD) of Amsterdam the 'sponsor'.

Investigators, these can be doctors or research nurses. They conduct the study at the Sexual Health Clinic (SHC) at the Public Health Service (GGD) of Amsterdam. GlaxoSmithKline plc (GSK) pays for the execution of this research, but has no role in the design, analyses, and interpretation of the study and results.

Participants in a medical study are often called subjects. Subject can be healthy subjects as well as patients.

This study needs 430 subjects that receive the HPV vaccine (Group 1) and 300 subjects that have not received the HPV vaccine (Group 2).This letter is written for participants of Group 1. The subjects are people that visit the Sexual Health Clinic (SHC) of the Public Health Service of Amsterdam in the Netherlands.

The Medical Ethics Review Committee of Academisch Medisch Centrum Amsterdam has approved this study.

2. What is the purpose of the study?

In this study we want to measure how often HPV infections are found in men who have sex with men (MSM) who received the medicinal product HPV vaccine (Cervarix) and how often the HPV infections are found in MSM that did not receive the HPV vaccination (Cervarix). We investigate this among MSM aged 19-26 years. We compare MSM who have not received the HPV vaccination (Group 2) with MSM who have received the HPV vaccination (Group 1). The HPV vaccine has been found to work well against HPV infections and is found to be safe. As a standard procedure, the safety of the vaccine will also be monitored.

3. What is the background of the study?

The RIVM (Rijksinstituut voor Volksgezondheid en Milieu) is inviting all men and women aged 19-26 years old for HPV vaccination in the calendar year 2023. This vaccine prevents new HPV infections. Some of these HPV infections can cause cervical, anal, penile, or head- and neck cancer several years later. In this study, we want to measure how often HPV infections are found in MSM who received the HPV vaccine and did not receive the HPV vaccine. The results are important to help plan vaccination approaches for the future.

4. What happens during the study?

The study consists of two periods during which MSM will be recruited.

In calendar year 2023 we will recruit MSM that are willing to receive the HPV vaccine (Group 1). The HPV vaccine will be offered free of charge by the Public Health Service (GGD).

How long will the study take?

Your participation in this study will be for about 24 months, counting from the first visit today up to the last visit 24 months later. During this period you will visit the Sexual Health Clinic (SHC) 3 times, and complete 3 online questionnaires.

Step 1: are you eligible to take part?

First, we want to know if you are eligible to take part. That is the reason that the investigator will ask you several questions to check if:

- You are born between 1996 and 2003
- You are male and you have had sex with another man during the preceding 6 months
- You have not been HPV vaccinated before
- You are able to read and understand Dutch or English
- You are not allergic to one or more components of the HPV vaccine
- You do not have a history of anal cancer or anal intraepithelial neoplasia (AIN)
- You agree to sign the informed consent

Group 1:

- You agree to receive the HPV vaccine
- You are willing and able to come to get the second HPV vaccination dose after 6 months
- You are willing and able to complete an online questionnaire after 15 months
- You are willing and able to return after 24 months for a final study visit
- You are not planning to relocate outside of Amsterdam region during the next 24 months

Please note: it is possible that you are not eligible for this study, even if you are healthy. The investigator will tell you more about this.

Step 2:

For this study, we will have 2 groups:

- Group 1. The people in this group will receive the HPV vaccination (Cervarix) in 2023.
- Group 2. The people in this group are participating in this study in calendar year 2025 and have not been HPV vaccinated (yet).

You are currently being recruited for Group 1.

The decision to get vaccinated against HPV is completely voluntary and you can decide for yourself if you want to do so.

Step 3: study and measurements
Group 1 (the HPV vaccinated group):
For this study, you need to physically visit the Sexual Health Clinic (SHC) 3 times over a period of 24 months. A visit lasts between 15 and 60 minutes. During the first and second visit (about 6 months apart) you will receive the HPV vaccination. During the first and last visit (which are 24 months apart) a nurse will ask you to provide a blood sample, an anal swab, a penile glans sample, and an oral swish-and-gargle sample. There will be five contact moments during which we will ask you to complete an online questionnaire. Completing this questionnaire will take you between 5 and 10 minutes. In Appendix B a schematic representation of the study measurements is provided, and a detailed description of what will happen during every contact moment.
Step 4: follow-up check
What is the difference with standard care?
This study is done in addition to the HPV vaccination routinely offered by the RIVM and the GGD. Normally, you would only receive the vaccination, but now we will measure how well the vaccine works and we will ask you about any discomforts you might have experienced after the vaccination.

5. What agreements do we make with you?

We want the study to go well. That is why we want to make the following agreements with you:

- You will receive the HPV vaccine according to the two-dose schedule as organized by the RIVM.
- You intend to go to all appointments.
- You should contact the investigator in these situations:
    - You are hospitalised or get treatment in a hospital.
    - You suddenly have problems with your health.
    - You no longer want to take part in the study.
    - Your telephone number, address or email address changes.
- You will receive an appointment card of the study. This card will contain your study number, contact details of the study staff, and your next appointment.

Is it OK for you or your partner to get pregnant during or after the study?
Do you have the desire to conceive a child? There are currently no fertility data available. However, studies do not indicate direct or indirect harmful effects with respect to fertility, pregnancy, embryonal/foetal development, parturition or post-natal development.

6. What side effects, adverse effects or discomforts could you experience?

The most common adverse reaction observed after the HPV vaccine administration was injection site pain; which occurred after 78% of all doses. The majority of these reactions were mild or moderate severity and were not long-lasting. Below we list several common and uncommon side effects.

If you experience any serious side effects first contact the closest emergency doctor or your general practitioner to resolve the acute situation. Please also notify the investigator immediately to have a medical doctor assess whether the serious side effect is causally related to the HPV vaccine.

The following side effects are very common:
Very common (side effects which may occur in more than 1 per 10 given doses of vaccine):

- pain or discomfort at the injection site
- redness or swelling at the injection site
- headache
- aching muscles, muscle tenderness or weakness (not caused by exercise)
- tiredness

Currently, there are no serious side effects caused by the HPV vaccine known.

More information about the HPV vaccine can be found in the information sheet, see appendix C

What are the possible discomforts you may experience with checks or measurements during the study?

- Taking a blood sample can be a little painful. In rare occasions, you could get a bruise as a result.
- Taking an anal or penile sample can be a little uncomfortable. A sample of the penis skin will be taken by rubbing the glans of the penis (externally).

7. What are the pros and cons if you take part in the study?

Taking part in the study can have pros and cons. We will list them below. Think about this carefully and talk to other people about it.

You yourself do not benefit from taking part in this study. Yet, if you take part you will help the investigators to get more insight into how well the HPV vaccine works in MSM aged 19-26 years. The results from this study will help decide whether it is relevant to provide the HPV vaccine routinely to MSM aged 19-26 years in the future. If you participate in this research and you receive the HPV vaccination, it does not mean that you will be cured of currently existing HPV infections.

The HPV vaccine protects against new HPV infections. You will only be protected against two types, i.e. HPV-16 and HPV-18.

Taking part in the study can have these cons:

- You may experience side effects of the HPV vaccine.
- There may be some discomfort from the measurements during the study.
- Taking part in the study will cost you extra time.

You do not wish to participate in the study?

It is up to you to decide if you wish to participate in the study. Independent of whether you do, or do not participate in this study, you can receive the HPV vaccination.

8. When does the study end?

The investigator will let you know if there is any new information about the study that is important to you. The investigator will then ask you if you want to continue to take part.

In these situations, the study will stop for you:

- All checks according to the schedule are finished.
- The end of the whole study has been reached for group 1 after 24 months
- You want to stop participating in the study yourself. You can stop at any time. Report this to the investigator immediately. You do not have to explain why you want to stop.
- The investigator thinks it is better for you to stop.
- One of the following authorities decides that the study should stop:
    - Public Health Service (GGD) of Amsterdam,
    - the government, or
    - the Medical Ethics Review Committee assessing the study

What happens if you stop participating in the study?

The investigators use the data and body material (for example to check whether you had or did not have anal HPV), that have been collected up to the moment that you decide to stop

participating in the study. If you wish, we will destroy the collected body material. Please let the investigator know.

The entire study ends when all the participants have finished. However, we will ask you if we may contact you in the future for any potential follow-up studies.

9. What happens after the study has ended?

Will you get the results of the study?

About three months after the last study participants have been recruited, the investigator will inform you about the most important results of the study. If you agreed, the investigator will also tell you whether your HPV vaccination has led to a good immune response by sharing with you your HPV serology status. If the HPV vaccine was not successful counselling will be provided, it is expected that unsuccessful vaccination will happen very rarely.

10. What will be done with your data and body material?

Are you taking part in the study? Then you also give your consent to collect, use and store your data and body material.

What data do we store?

We store these data:

- your name
- your gender
- your address
- your date of birth
- information about your health
- information about medication you use
- (medical) information that we collect during your visit at the SHC (among which sexually transmitted infection [STI] status,vaccination status and medication use)

What body material do we store?

We collect, use and store tubes of blood and anal swab, a penile glans sample, and an oral swish-and-gargle sample.

Why do we collect, use and store your data and body material?

We collect, use and store your data and your body material to answer the questions of this study. And to be able to publish the results. Data and/or body material can be used by the sponsor and research institutes that help the sponsor with the practical performance, the analysis of data, and measurements on tissue samples.

How do we protect your privacy?
To protect your privacy, we give a code to your data and your body material. We only put this code on your data and body material. We keep the key to the code in a safe place in a protected environment on the server and a locked closet in a locked room at the Public Health Service (GGD) of Amsterdam. When we process your data and body material, we always use only that code. Even in reports and publications about the study, nobody will be able to see that it was about you.

Who can see your data?
Some people can see your name and other personal information without a code. This could include data specifically collected for this study, but also data from your medical file. These are people checking whether the investigators are carrying out the study properly and reliably. These persons can access your data:

- An auditor who is hired by the Public Health Service (GGD) of Amsterdam.
- National and international supervisory authorities.
- Research nurses and medical doctors of the research team of the Public Health Service of Amsterdam.

These people will keep your information confidential. We ask you to give permission for this access. The Health and Youth Inspectorate can access your personal information without your permission.

For how long do we store your data and body material?
We store your data at the Public Health Service for 25 years. Your body material will be stored for 10 years. It will be stored for this period in order to perform new analyses related to this study in the course of this study. If no longer needed, we will destroy your body material.

Can we use your data and body material for other research?
Your collected data and your (remaining) body material may also be important for other medical research about infectious diseases. For this purpose, your data will be stored for 25 years and your body material for 10 years at the Public Health Service (GGD) of Amsterdam. Please indicate in the consent form whether you agree with this. Do you not want to give your consent? Then you can still take part in this study. You will get the same healthcare.

Can you take back your consent for the use of your data?
You can take back your consent for the use of your data at any time. Please tell the investigator if you wish to do so. This applies both to the use in this study and to the use in other medical research. But please note: if you take back your consent, and the investigators have already collected data for research, they are still allowed to use this information. The investigators will destroy your body material after you take back your consent. But if assessments with your body material have been carried out, the investigator can continue to use the results.

Do you want to know more about your privacy?

- Do you want to know more about your rights when processing personal data? Visit www.autoriteitpersoonsgegevens.nl.
- Do you have questions about your rights? Or do you have a complaint about the processing of your personal data? Please contact the person who is responsible for processing your personal data. For the present, this is:
    - Public Health Service of Amsterdam. See Appendix A for contact details, and website.
- If you have any complaints about the processing of your personal data, we recommend that you first discuss them with the research team. You can also contact the Data Protection Officer of Public Health Service of Amsterdam. Or you can submit a complaint to the Dutch Data Protection Authority.

Where can you find more information about the study?
You can find more information about the study on the following website: https://euclinicaltrials.eu/ . After the study, the website may show a summary of the results of this study. You can find the study by searching for '2022-502224-49-00' .

11. Will you receive compensation if you participate in the study?

The HPV vaccine is offered by the RIVM and the GGD. Additional tests done by the study will not cost you anything. Neither will you get any compensation.

12. Are you insured during the study?

You are not additionally insured for this study. This is because taking part in the study has no additional risks. That is why the Public Health Service (GGD) Amsterdam, following advice from the medical ethics review committee of the Amsterdam UMC, does not have to take out additional insurance.

13. We will not inform other organizations about your participation.

No other organizations will be informed about your participation.

14. Do you have any questions?

You can ask the investigators of the research team questions about the study.

Would you like to get advice from someone who is independent from the study? Then contact the independent expert, for contact details go to appendix A. He knows a lot about the study, but is not a part of this study.

Do you have a complaint? Discuss it with the investigators of the research team. If you prefer not to do so, please contact the complaints coordinator of GGD Amsterdam or the privacy officer of GGD Amsterdam or the Dutch Data Protection Authority. Appendix A tells you where to find this.

15. How do you give consent for the study?

You can first think carefully about this study. Then you tell the investigator if you understand the information and if you want to take part or not. If you want to take part, fill in the consent form that you can find with this information sheet. You and the investigator will both get a signed version of this consent form.

Thank you for your attention.

16. Appendices to this information

Appendix A: contact details for Public Health Service of Amsterdam

Principal investigator:
Name: <<not visible for CTIS submission reason>>
Role: Senior Epidemiologist, Public Health Service of Amsterdam
Phone: <<not visible for CTIS submission reason>>
Availability: Monday through Friday from 9:00 to 17:00

Research nurse:
Name: <<not visible for CTIS submission reason>>
Phone: <<not visible for CTIS submission reason>>
Availability: Monday through Friday from 9:00 to 17:00

Independent expert:
Name:<<not visible for CTIS submission reason>>,
Role: Independent expert and physician
Phone: <<not visible for CTIS submission reason>>
Availability: Monday through Friday from 9:00 to 17:00

Complaints: You can find the ways to contact the complaints office at https://www.ggd.amsterdam.nl/ggd/klachten/ (in Dutch). Or send email to klachten@ggd.amsterdam.nl.

Privacy Officer of the institution: <<not visible for CTIS submission reason>>
can be contacted through email: <<not visible for CTIS submission reason>>
@ggd.amsterdam.nl

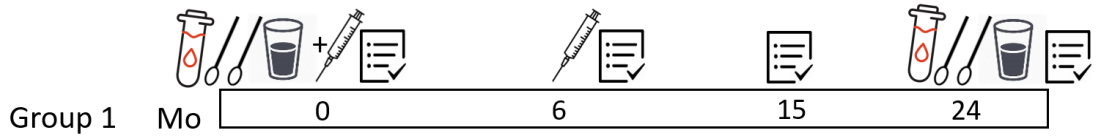
For more information about your rights regarding privacy:
https://www.ggd.amsterdam.nl/privacy-ggd-amsterdam/algemene-privacyverklaring-ggd-amsterdam/

If you have any questions, objections or comments about the processing of your personal data, you can ask the study staff (hpvman@ggd.amsterdam.nl).

Coordinating investigator:
Name:<<not visible for CTIS submission reason>>,
Role: Postdoctoral Epidemiologist, Public Health Service of Amsterdam
Phone: <<not visible for CTIS submission reason>>
Availability: Monday through Friday from 9:00 to 17:00

For emergency:
For emergencies call the national emergency number 112

Appendix B: Overview of measurements



Schematic representation of study measurements.

Group 1:

1st contact (visit at the SHC): The investigator of the research team (a research nurse or a medical doctor) will explain you how to take an anal swab, a penile glans sample, and an oral swish-and-gargle sample. The investigator will take 5 mL venous blood. In addition to the questions asked during your regular consultation we will ask you to complete an additional questionnaire. The questions used for this study concern some general information and about your, general health, sexual behaviour, and use of alcohol, drugs, and tobacco. It will take you around 5-10 minutes to complete this questionnaire. After all the samples have been collected a nurse or medical doctor will administer your first HPV vaccine dose in your non-dominant upper arm. In total, this visit will last around 60 minutes.

2nd contact (online): Fourteen days after the HPV vaccination you will receive a message with a link to an online questionnaire. The questions are about symptoms you may have experienced after you received the HPV vaccine. It will take you around 5-10 minutes to complete this questionnaire.

3rd contact (visit at the SHC): During this visit, a nurse or doctor's assistant will give you the second HPV vaccination in your upper arm. This visit will last 15 minutes. During this visit, you do not need to provide any samples nor complete a questionnaire.

4th contact (online): Fourteen days after the HPV vaccination you will receive a message with a link to an online questionnaire. The questions are about symptoms you may have experienced after you received the HPV vaccine. It will take you around 5-10 minutes to complete this questionnaire.

5th contact (online): Fifteen (15) months after your first visit you will receive an online questionnaire regarding symptoms you may have felt after you received the HPV vaccine, general health and sexual behaviour. It will take you around 5-10 minutes to complete this questionnaire.

6th contact (visit at the SHC): Twenty four (24) months after your first visit a last physical visit will be planned. During this visit, the investigators of the research team will explain you how to take an anal swab, a penile glans sample, and an oral swish-and-gargle sample. The investigator will take 5 mL venous blood. In addition to the questions asked during your regular consultation we will ask you to complete an additional questionnaire. The questions used for this study concern demographic characteristics, general health, sexual behaviour, and use of alcohol, drugs, and tobacco. It will take you around 5-10 minutes to complete this questionnaire. In total, this visit will last around 60 minutes.

Appendix C - Side Effects, Adverse Effects and Discomforts

The following side effects are common (side effects which may occur in less than 1 per 10 but more than 1 per 100 doses of vaccine administered):

- gastrointestinal symptoms including nausea, vomiting, diarrhoea, and abdominal pain
- itching, red skin rash, hives (urticaria)
- joint pain
- fever (≥38°C)

The following side effects are uncommon (side effects which may occur in less than 1 per 100 but more than 1 per 1,000 doses of vaccine administered):

- upper respiratory tract infection (infection of the nose, throat or trachea)
- dizziness
- other injection site reactions such as hard lump, tingling, or numbness.

Appendix D: Informed consent form – subject

Belonging to

Human papillomavirus (HPV) vaccine effectiveness study among men who have sex with men (HPV4M)

- I have read the information sheet. I was able to ask questions. My questions have been answered well enough. I had enough time to decide if I wanted to take part.
- I know that taking part is voluntary. I also know that at any time I can decide not to take part in the study. Or to stop taking part. I do not have to explain why.
- I give the investigator consent to inform the RIVM *(Rijksinstituut voor Volksgezondheid en Milieu / National Institute for Public Health and the Environment)* about my HPV vaccination status.
- I give consent to collect and use my routinely collected and study collected data and body material. The investigators only do this to answer the question of this study.
- I know that some people will be able to see all of my data to review the study. These people are mentioned in this information sheet. I give consent to let them see my data for this review.
- I know that if I want to conceive a child I am encouraged to postpone this if I receive the HPV vaccine, which is 6 months after my last HPV vaccination.
- Please tick yes or no in the table below.

I give consent to store my data to use for other research, as stated in the information sheet.	Yes ☐	No☐
I give consent to have my (remaining) body material stored for use in other research, as stated in the information sheet. The body material is stored for this purpose for another 10 years.	Yes ☐	No☐
I give consent to ask me after this study if I want to participate in a follow-up study.	Yes ☐	No☐
I give consent to contact me after the study with the most important results and whether my HPV vaccination has led to a good immune response.	Yes ☐	No☐

- I want to take part in this study.

My name is (subject): ……..

Signature: …… Date : __/__/__

I declare that I have fully informed this subject about the study mentioned.

If any information becomes known during the study that could influence the subject's consent, I will let this subject know in good time.

Investigator name (or their representative): .....
Signature:…… Date: __/__/__

Additional information was given by:
Name:……..
Job title:……
Signature:…… Date: __/__/__

The study subject will receive a complete information sheet, together with a signed version of the consent form.