

# Human papillomavirus infection: a randomised controlled trial of Imiquimod cream (5%) versus Podophyllotoxin cream (0.15%), in combination with quadrivalent human papillomavirus or control vaccination in the treatment and prevention of recurrence of anogenital warts

<b>Submission date</b> 25/07/2014	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 25/07/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 28/09/2020	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Genital warts are a very common sexually transmitted disease and are caused in over 90% of cases by human papillomavirus (HPV) types 6 or 11. Podophyllotoxin (as a cream or solution) and imiquimod cream are the most frequently used topical treatments for genital warts, but they have never been adequately compared to determine their relative effectiveness with respect to the clearance or recurrence rate. A vaccine is available to prevent HPV 6 and 11 (as well as HPV 16 and 18, the viruses that cause most cervical cancer), but it is not known whether it will increase the rate of clearance of genital warts if it is given at the same time as topical treatment, or whether it can prevent recurrences. The aim of this study is to find out whether imiquimod or podophyllotoxin is more effective at clearing and preventing recurrence of genital warts, and whether the addition of HPV vaccination provides additional benefits.

### Who can participate?

Patients aged 18 or over with genital warts

### What does the study involve?

Participants are randomly allocated to be treated with either imiquimod cream or podophyllotoxin cream, and to be treated with either a course of quadrivalent HPV vaccine (active against HPV types 6/11/16/18) or a placebo (dummy injection). This results in four treatment groups: imiquimod cream plus HPV vaccine; podophyllotoxin cream plus HPV vaccine; imiquimod cream plus placebo vaccine; and podophyllotoxin cream plus placebo vaccine. Successful treatment is defined as clearance of warts after 16 weeks and no relapse between 16 and 48 weeks. The study also compares the time taken for warts to be cleared with each treatment, the number of patients switching treatment because of non-response to treatment

or side-effects, and the patients' quality of life. An analysis is also conducted to compare the cost effectiveness of each treatment. Imiquimod is currently more expensive than podophyllotoxin (although the cost difference is expected to reduce). The economic benefit of HPV vaccination is also studied.

What are the possible benefits and risks of participating?  
Not provided at time of registration

Where is the study run from?  
University College London (UK)

When is the study starting and how long is it expected to run for?  
June 2014 to March 2017

Who is funding the study?  
Health Technology Assessment Programme (UK)

Who is the main contact?  
Dr Macey Murray  
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## Contact information

**Type(s)**  
Scientific

**Contact name**  
Dr Macey Murray

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
2013-002951-14

**Protocol serial number**  
16857; HTA 11/129/187

## Study information

**Scientific Title**

Human papillomavirus infection: a randomised controlled trial of Imiquimod cream (5%) versus Podophyllotoxin cream (0.15%), in combination with quadrivalent human papillomavirus or control vaccination in the treatment and prevention of recurrence of anogenital warts (HIPvac Trial)

## **Acronym**

HIPvac

## **Study objectives**

The HIPvac trial will address two questions regarding the management of patients with genital warts. The first is which of the two most frequently used creams used to treat warts, imiquimod or podophyllotoxin, is most effective at clearing genital warts, and preventing recurrence. The second is whether a course of human papillomavirus (HPV) vaccine started at the time of initiating topical treatment, increases the effectiveness of the cream in either clearing the warts or preventing recurrence. The HPV vaccine used is licensed for the prevention of infection caused by HPV 6 and 11 (which cause 90% genital warts) and HPV 16 and 18 (cause 70% cervical cancer). The vaccine is used in the national vaccination programme in the UK for girls aged 12-13; it is not licensed for the treatment of genital warts.

More details can be found at: <http://www.nets.nihr.ac.uk/projects/hta/11129187>

Protocol can be found at: [http://www.nets.nihr.ac.uk/\\_\\_data/assets/pdf\\_file/0007/94642/PRO-11-129-187.pdf](http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0007/94642/PRO-11-129-187.pdf)

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

13/SC/0638; First MREC approval date 03/02/2014

## **Study design**

Randomised; Interventional; Design type: Not specified, Treatment

## **Primary study design**

Interventional

## **Study type(s)**

Treatment

## **Health condition(s) or problem(s) studied**

Topic: Infectious diseases and microbiology; Subtopic: Infection (all Subtopics); Disease: Infectious diseases and microbiology

## **Interventions**

The trial will follow participants for 48 weeks (6 visits). They will be randomly assigned to one of the creams (imiquimod 5% or podophyllotoxin 0.15%). Patients will know which cream they have been given as the creams have different dosing schedules. The creams will be used per standard care. The vaccine will be randomly assigned at the same time. Participants will receive either HPV vaccine (Gardasil) or placebo (saline injection). Patients will receive three doses of vaccine, the first at their baseline visit, then at week 8 and 24.

## **Intervention Type**

Mixed

## **Primary outcome(s)**

Wart clearance within 16 weeks of starting treatment and remaining wart-free between 16 and 48 weeks

## **Key secondary outcome(s)**

1. Proportion wart-free at the end of the assigned treatment course; Timepoint(s): 4 or 16 weeks
2. Proportion experiencing wart recurrence/relapse after complete wart clearance; Timepoint(s): Up to 48 weeks
3. Time from complete wart clearance to recurrence/relapse; Timepoint(s): Up to 48 weeks
4. Adverse events; Timepoint(s): As required
5. Health-related quality of life, as measured by the Area Under the Curve for EQ-5D; Timepoint(s): At all visits
6. Symptom scores; Timepoint(s): At all review of treatment visits
7. Total costs of treatment including prescribed agents and clinic visits; Timepoint(s): 48 weeks
8. Proportion wart-free at 16 weeks, with use of additional treatment as required; Timepoint(s): 16 weeks
9. Quantity of additional treatment required to achieve clearance by 16 weeks; Timepoint(s): 16 weeks
10. Proportion wart-free at 24 weeks; Timepoint(s): 24 weeks
11. Proportion wart-free at 24 weeks with use of additional treatment as required; Timepoint(s): 24 weeks
12. Quantity of additional treatment required to achieve clearance by 24 weeks; Timepoint(s): 24 weeks
13. Proportion experiencing wart recurrence/relapse at 48 weeks after wart clearance at 24 weeks; Timepoint(s): 24, 48 weeks
14. Proportion experiencing complete wart clearance; Timepoint(s): 48 weeks
15. Time to complete wart clearance; Timepoint(s): Point of wart clearance

## **Completion date**

31/03/2017

## **Eligibility**

### **Key inclusion criteria**

1. Age 18 years or over
2. Males and females
3. First episode or repeat episode of anogenital warts diagnosed clinically
4. External anogenital warts considered, in the opinion of the investigator, to be suitable for self-administered topical wart treatment (patients with concurrent internal anogenital warts are still eligible to participate)
5. Able to provide informed consent to participate in the trial

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Total final enrolment**

503

**Key exclusion criteria**

1. Previous wart treatment in the last 3 months
2. Previous quadrivalent HPV vaccine (previous bivalent HPV vaccine is not an exclusion criterion)
3. Previous intolerance to either of the topical treatments, vaccines or their constituents
4. Known HIV-positivity (HIV testing is not required for the trial)
5. Pregnancy or lactation (current, or planned in the next 6 months)
6. Women of child bearing potential not willing to use effective contraception for the duration and 30 days post completion of trial treatment: see above
7. Unable or unwilling to complete follow-up procedures
8. Lesion area greater than 4 cm<sup>2</sup>, requiring treatment under direct supervision of medical staff (in accordance with podophyllotoxin cream Summary of Product Characteristics)
9. Patients who have had topical steroids applied to the target area, or systemic steroids or other immunosuppressive agents, within 1 month prior to randomisation
10. Patients enrolled in any other trial of an Investigational Medicinal Product, without the permission of the Chief Investigator
11. Any clinical condition which the investigator considers would make the patient unsuitable for the trial, including immunodeficiency conditions

**Date of first enrolment**

30/06/2014

**Date of final enrolment**

31/03/2017

**Locations****Countries of recruitment**

United Kingdom

England

**Study participating centre**

University College London

London

United Kingdom

WC1E 6BT

# Sponsor information

## Organisation

University College London (UK)

## ROR

<https://ror.org/02jx3x895>

# Funder(s)

## Funder type

Government

## Funder Name

Health Technology Assessment Programme

## Alternative Name(s)

NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

## Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

United Kingdom

# Results and Publications

## Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date

## IPD sharing plan summary

Data sharing statement to be made available at a later date

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/09/2020	28/09/2020	Yes	No

<a href="#">Protocol article</a>	protocol	06/11/2018	Yes	No
<a href="#">Basic results</a>			No	No
<a href="#">HRA research summary</a>		28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No
				Yes