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Adding male single-dose HPV vaccination to female HPV vaccination in Tanzania

Submission date
10/07/2023

Recruitment status
Recruiting

Registration date
14/07/2023

Overall study status
Ongoing

Last Edited
14/07/2023

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Human papillomavirus (HPV) infection is the primary cause of cervical cancer, a major public health problem in Africa. Vaccinations available offer excellent protection against HPV infection with vaccine-related HPV genotypes. A call in 2018 by the World Health Organisation (WHO) to eliminate cervical cancer will require novel approaches to protect unvaccinated individuals from HPV infection, in addition to approaches that increase vaccine coverage in girls. A potential approach is to offer vaccination to boys to protect unvaccinated girls through herd immunity and hence reduce the population prevalence of HPV infection. The London School of Hygiene and Tropical Medicine (LSHTM; the sponsor) and the Mwanza Intervention Trials Unit (MITU) are evaluating the effectiveness of a single dose of the 4-valent prophylactic human papillomavirus (HPV) vaccine (Gardasil®) given to males alongside the national HPV vaccination programme of females in reducing population prevalence of HPV in Tanzania. The main objective of the study is to measure the impact of adding a one-time single-dose male HPV vaccination strategy to the national HPV vaccination programme in girls on the population prevalence of HPV vaccine genotypes in 18 to 21-year-old males and females.

Who can participate?
Boys aged between 14 to 18 years old and girls aged 14 years old in 26 communities/clusters (13 per arm) in the Lake Victoria region of Tanzania

What does the study involve?
The study is an unblinded study with two arms:
1. The national HPV vaccination programme (control arm)
2. The national programme plus male HPV vaccination is given to a multi-year cohort of boys (intervention arm).
All boys in the intervention arm will be eligible to receive one dose of the 4-valent HPV vaccine (Gardasil®). All girls in both arms are offered HPV vaccination with the 4-valent HPV vaccine through the national HPV vaccination programme.

Genital HPV prevalence in 18 to 21-year-olds will be compared between control and intervention clusters at baseline (prior to vaccination of boys) and 36 months after vaccination of boys. All individuals aged 18-21 years old who are residents in the communities will be eligible to

participate in the survey. Blood sampling for immune responses and adverse event data collection will be performed in a subset of 200 vaccinated male subjects (the immunogenicity cohort) in selected intervention clusters.

For the cross-sectional surveys, the study involves a short interview where socio-demographic, health and sexual behaviour details will be collected, and the collection of two nurse-assisted self-administered genital swabs for testing for HPV infection. For the vaccination phase, consenting boys will be administered a single dose of HPV vaccine via intra-muscular injection into the deltoid region of the upper arm. Boys who consent to participate in the immunogenicity cohort will be asked to attend a follow-up visit at M1, 12, 24 and 36 post-vaccination, and a blood sample will be taken for immunogenicity testing.

What are the possible benefits and risks of participating?
Participants who are part of the HPV prevalence surveys will benefit from a free health check-up and free treatment if the clinician thinks they may have a reproductive tract Infection. Boys who take part in the trial will benefit from getting a free medical check-up too, and one dose of the HPV vaccination. For the immunogenicity cohort, testing the blood samples will help in understanding the immune response after a single dose of the HPV vaccine among boys in Sub-Saharan Africa and see if they have the same level of immunity against HPV as girls in the same region. This will help in developing better mechanisms of delivering HPV vaccine to protect people and ultimately potentially provide herd immunity against HPV infection.
The risks of the study are small. There may be a small risk of allergic reaction or other side effects (as with all vaccines), stigmatisation due to vaccination or participation in research, pain or bruising during blood taking or minor discomfort or embarrassment during the collection of genital swabs. Study procedures are carried out by trained and qualified staff, who have been carefully trained in procedures to minimise social and other harms. All participants who have been vaccinated must wait for 30 mins after vaccination for observation and participants and their parents will be strongly advised to report any suspected adverse effects promptly.

Where is the study run from?
London School of Hygiene & Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
December 2019 to December 2026

Who is funding the study?
1. Medical Research Council (UK) through the Joint Global Health Trials funding scheme
2. Merck & Co (USA)

Who is the main contact?
Professor Deborah Watson-Jones (Chief Investigator), deborah.watson-jones@lshtm.ac.uk

Contact information

Type(s)
Principal investigator

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
NCT04953130

Protocol serial number
MITU-003

Study information

Scientific Title
The population-level impact of adding male single-dose HPV vaccination to female HPV vaccination in Tanzania: a cluster-randomised trial

Acronym
Add Vacc

Study objectives
Adding single-dose male HPV vaccination to the Tanzanian national HPV vaccination programme in girls will reduce the population prevalence of HPV vaccine-genotype infection.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 10/09/2021, Tanzanian Medical Research Coordinating Committee (MRCC) (2448 Ocean Road P.O. Box 9653, Dar es Salaam, None available, Tanzania; +255 22 2121400; nimrethics@gmail.com), ref: NIMR/HQ/R.8a/Vol.IX/3785

2. approved 19/07/2021, London School of Hygiene & Tropical Medicine Ethics Committee (London School of Hygiene & Tropical Medicine, Keppel Street, London, WC1E 7HT, United Kingdom; +44(0)2076368636; ethics@lshtm.ac.uk), ref: 25784

Study design
Unblinded cluster-randomized controlled trial with 2 arms conducted in 26 communities

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of cervical cancer and other cancers associated with human papillomavirus (HPV) infection

Interventions
26 communities in the Lake Victoria zone of Tanzania were randomly allocated to one of two arms:
1. The national HPV vaccination programme (girls aged 14 years old, control)
2. The national programme plus male single-dose HPV vaccination given to a multi-year cohort of boys (intervention arm)
All males aged 14 to 18 years old in the intervention arm (approximately 880, on average, per community and up to 13,000 in total) are eligible to receive one dose of the 4-valent HPV vaccine (Gardasil®) that protects against HPV 6, 11, 16, and 18. In the control arm, all girls aged 14 years old are eligible to receive two doses of the same vaccine (Gardasil®), given at 0 and 6 months, through the national HPV vaccination programme. Communities were randomly allocated 1:1 to the intervention and control arms (13 per arm), stratified on population size (<14,000 or ≥14,000) and the estimated coverage of at least one dose of HPV vaccine among girls aged 14-18 (<24.3% or ≥24.3%). Restricted randomisation was used to ensure the balance

between arms on the following covariates: the number of primary schools; the proportion of households residing in the community for <5 years; the proportion of households with <5 members in the household; the number of lifetime partners among men and women aged 18-21 years; the proportion of men and women aged 18-21 years who report having a partner in the past 3 years who lived outside the community.

Intervention Type
Biological/Vaccine

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Gardasil® HPV vaccine that protects against infection with HPV genotypes 6, 11, 16, and 18 (manufacturer Merck)

Primary outcome(s)
The proportion of females and males aged 18 to 21 years in each arm with detectable genital 4-valent HPV vaccine genotype DNA (HPV 6, 11, 16 or 18) measured by a cross-sectional population survey using a validated PCR assay at month 36

Key secondary outcome(s))
1. In a cohort of vaccinated boys, the proportion seroconverting to, and geometric mean antibody concentrations for HPV vaccine genotypes (HPV6, 11, 16 and 18) measured using pseudovirion (PsV)-based antibody Luminex assay at 1, 12 and 24 months post-vaccination
2. In a cohort of vaccinated boys, safety and tolerability (local and systemic adverse events) measured using self-reporting at 1, 12, and 24 months post-vaccination
3. The proportion of females and males aged 18 to 21 years in the control arm with detectable genital 4-valent HPV vaccine genotype DNA (HPV 6, 11, 16 or 18) measured with cross-sectional population surveys using a validated PCR assay at baseline and month 36
4. The proportion of females eligible for the national HPV vaccination programme in each arm who received 1 dose of HPV vaccine (uptake) and who completed 2 doses (coverage) measured using cross-sectional population surveys at baseline and month 36
5. The cost-effectiveness of adding a single-dose male vaccination to an existing female vaccination programme measured using a standardized HPV vaccine costing tool at month 36
6. Acceptability of a gender-neutral approach to HPV vaccination measured through a qualitative survey at month 36

Completion date
31/12/2026

Eligibility

Key inclusion criteria
For population surveys in all clusters (baseline and endline):
1. Participants must sign an informed consent form (ICF) indicating that he or she understands the purpose of, and procedures required for, the study and is willing to participate in the study. If the participant cannot read or write, the procedures must be explained and informed consent must be witnessed by a trusted literate third party who is not involved with the conduct of the study
2. Participants must be a man or woman who has lived in that community for at least 3 years and

who is aged between 18 and 21 years, inclusive
3. Participants must be willing and able to comply with the protocol requirements
4. Participants must have a means to be contacted

For vaccination:
1. Parents and adult male participants (aged 18 years) must sign an ICF and male participants aged less than 18 years must sign an informed assent form (IAF), indicating that they understand the purpose of and procedures required for the study and are willing to participate in the study and to receive HPV vaccination. If the parent or participant cannot read or write, the procedures must be explained and informed consent/assent must be witnessed by a literate third party who is not involved in the conduct of the study
2. Participants must have been born male, and must be aged 14 to 18 years inclusive at time of vaccination
3. Participants must be living in an intervention community (cluster)
4. Participants must be willing and able to comply with the protocol requirements
5. Participants must agree to avoid all non-trial immunisations in the 14 days following vaccination with the trial vaccine, other than emergency vaccinations such as post-exposure rabies or tetanus vaccinations
6. Participants must be healthy as determined by a medical history. A physical examination will be conducted if necessary according to the clinician's judgement

Participant type(s)
Healthy volunteer, Resident, Other

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
14 years

Upper age limit
21 years

Sex
All

Key exclusion criteria
Men and women will be excluded from survey participation if they:
1. Are temporary visitors in a study community
2. Have one or more medical reasons why a swab cannot be taken from the genitals
3. Have an acute illness that precludes participation. (In such cases, participants may be rescreened for participation at a later date if the illness resolves within the survey period within that community)
Females will be excluded if they report menstruation on the day of the interview and sample collection. In such cases, participants may be re-considered for inclusion at a later date if menstruation ceases within the survey period within that community or during mop-up activities.

Boys will be excluded from HPV vaccination if:
1. They have previously been vaccinated against HPV
2. They have a history of allergy or anaphylaxis to one or more of the HPV vaccine components, to yeast or to latex
3. They are enrolled in another vaccine research study that specifically specifies that they must not participate in a study of another vaccine
4. They have been diagnosed with a chronic condition (except HIV, as per the comment above), such as an autoimmune condition, sickle cell disease, degenerative disease, neurologic or genetic disease, among others
5. There are significant conditions or clinically significant findings for which, in the opinion of the investigator, participation would not be in the best interest of the participant (e.g., it would compromise their safety or well-being)

Date of first enrolment
01/08/2022

Date of final enrolment
30/09/2026

Locations

Countries of recruitment
Tanzania

Study participating centre
Mwanza Intervention Trials Unit (MITU)
Isamilo Road, P.O. Box 11936
Mwanza
Tanzania
N/A

Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Merck Sharp and Dohme

Alternative Name(s)
MSD United Kingdom, Merck Sharp & Dohme, Merck Sharp & Dohme Corp., MSD

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available on request from the MITU Data Access Committee and the study Principal Investigator Prof Deborah Watson-Jones, deborah.watson-jones@lshtm.ac.uk, following MITU's data sharing policy. Consent for sharing data with other researchers will be obtained from participants.

IPD sharing plan summary
Available on request