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Field trial of a novel point-of-care HPV 'self-collect, test and treat' cervical screening strategy for women in low- and middle-income countries: the HPV-STAT study, Papua New Guinea

Submission date	**Recruitment status**	[_] Prospectively registered
11/09/2018	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
25/09/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
26/07/2022	Cancer	

Plain English summary of protocol

Background and study aims

Cancer of the cervix is the most common cancer in women in many developing countries, including Papua New Guinea. If detected early enough, cervical cancer can be cured. Unfortunately, the majority of women in many developing countries do not know they have cervical cancer until it is too late, when the disease cannot be cured. In Papua New Guinea, screening for cervical cancer using Pap smear testing has proved difficult especially in rural areas, because women find it too hard to return to the clinic for their test results. Screening efforts based on an internal examination and the application of dilute vinegar to the cervix to identify early stage disease (known as VIA) have also been disappointing.

Recent studies in countries across the world have shown that screening women for the virus that causes cervical cancer (the human papillomavirus or HPV) can help detect cancer at an early stage and save lives. This study will look at a new way to screen for cervical cancer. In this study, women in Papua New Guinea will be tested for HPV infection when they come to clinic. Women will be given their test results the same day. Women having a positive HPV test will have an internal examination and offered same-day curative treatment.

Who can participate?

Adult women aged 30-59 years who attend Well Woman Clinics in Alotau, Kokopo, Madang, and Mt Hagen, Papua New Guinea.

What does the study involve?

A total of around 4000 women will be asked to take part in the study. Women will be asked some questions about their general health and their sexual and reproductive health. Participants will also be asked to provide a self-collected vaginal specimen for HPV testing that will be conducted in the clinic on the same day. Each HPV test will take around 60 minutes to complete. HPV test results will be provided to women on the same day.

Women who have a positive HPV test will be asked to undergo an internal examination and will be offered curative treatment. During the examination, an additional specimen for laboratory testing will be collected from the cervix. This specimen will be sent to Australia where it will be looked at in a specialist laboratory to see if there is cervical pre-cancer or cancer present. The cervix will be treated using either a freezing device (cryotherapy) or a heating device (thermocoagulation). Women will be asked to come back to the clinic for review in 3 months and 12 months' time. At the 3 month review, women will be given the results of laboratory tests carried out in Australia.
Women who have a negative HPV test will be advised that no further examination or treatment is required but that they should return for repeat screening in 3 years' time. Some HPV negative women (around 15%) will be asked to provide additional specimens for laboratory testing in Australia, as described above. This will allow the study team to compare test results between HPV positive and negative women. These women will also be asked to come back to the clinic in 3 months' time when they will be given the results of the additional laboratory tests carried out in Australia.
Finally, some women may be asked to take part in an additional interview or a small group discussion. These will help us understand what women think about the care they received, and the costs involved in coming to the clinic for screening.

What are the possible benefits and risks of participating?
The study will provide valuable information for researchers, health staff and policy makers seeking to improve the sexual health of women, families and communities in PNG. Women who participate in the study may benefit directly from taking part as a result of receiving an HPV test and any treatment that they receive.
There are no risks involved in collecting genital swabs and testing them for HPV infection. Women who undergo cervical treatment may experience mild-to-moderate discomfort when the treatment is being given in the clinic. They may also experience a small amount of vaginal discharge, or might notice some small spots of blood in their underwear ('spotting') for up to one-week following the procedure. Women who receive treatment will be advised to abstain from sexual intercourse until all discharge has ceased. Some women may feel slightly uncomfortable or embarrassed when asked questions about their sexual health. All study interviewers are trained staff with experience in asking such questions and will do their best to avoid any such feelings arising during the study.

Where is the study run from?
Papua New Guinea Institute of Medical Research (PNGIMR) (Papua New Guinea)

When is the study starting and how long is it expected to run for?
July 2017 to March 2021

Who is funding the study?
National Health and Medical Research Council (NHMRC) (Australia)

Who is the main contact?
Dr Andrew Vallely
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Nil known

Study information

Scientific Title
Prospective cohort study to evaluate point-of-care HPV-DNA testing for the early detection and treatment of cervical pre-cancer in high-burden, low-resource settings

Acronym
HPV-STAT

Study objectives
Point-of-care HPV-DNA testing is effective, cost-effective, acceptable to women and health providers and can be scaled up within existing health systems for primary cervical screening in low- and middle-income countries.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Papua New Guinea Institute of Medical Research (PNGIMR) Institutional Review Board (IRB), 12/04/2018, IRB No. 1712
2. Papua New Guinea National Department of Health Medical (NDoH) Research Advisory Committee (MRAC), 05/06/2018, MRAC No. 17.36
3. University of New South Wales (UNSW) Human Research Ethics Committee (HREC), 21/02/2018, HREC No. HC17631

Study design
Observational prospective multi-centre longitudinal cohort study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Other

Study type(s)
Screening

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Cervical pre-cancer and cervical cancer

Interventions
Point-of-care HPV-DNA testing using self-collected vaginal specimens tested on the Cepheid GeneXpert platform (Xpert HPV Test). Women having a positive HPV test result are offered a pelvic examination and same-day cervical ablation using cryotherapy or thermocoagulation. Visualisation of the cervical transformation zone prior to ablation is aided by the application of dilute vinegar (acetic acid) as per current international and national guidelines for the conduct of visual inspection with acetic acid (VIA).
At enrolment, women will be offered same day HPV-DNA testing, and treatment if HPV positive. Women who are HPV positive plus a 15% randomly selected sub-population of HPV negative women will be asked to provide additional cervical specimens for off-site liquid based cytology (to be conducted in Melbourne), and to re-attend in three-months.
Women who were HPV positive at enrolment, plus a 15% randomly selected sub-population of women who were HPV negative at enrolment, will be asked to re-attend to receive baseline cytology results.
Women who were HPV positive at enrolment will be asked to re-attend for repeat HPV-DNA testing and clinical review as indicated.
Some women may be asked to take part in an additional interview or a small group discussion. These will help us understand what women think about the care they received, and the costs involved in coming to the clinic for screening.

Intervention Type
Other

Primary outcome measure
The performance of the Xpert HPV Test for the detection of underlying high-grade intraepithelial lesions (HSIL) when provided at point-of-care using self-collected vaginal specimens. Performance for the detection of underlying HSIL will be evaluated using the following standard diagnostic evaluation criteria:
1. Sensitivity
2. Specificity
3. Positive predictive value

4. Negative predictive value
We will calculate the sensitivity, specificity, positive and negative predictive values (with 95% confidence intervals) of the Xpert HPV Test to detect HSIL.
Performance will be evaluated at enrolment.

Secondary outcome measures
The following will be assessed at the baseline, around 3-6 months after enrolment (study mid-point) and 12-18 months after enrolment (end of the trial):
1. Cost-effectiveness of point-of-care Xpert HPV testing for the early detection and treatment of cervical pre-cancer lesions. Standard cost-effectiveness analyses will be performed by identifying the cost-effectiveness frontier and calculating the incremental cost-effectiveness ratios (ICERs) of strategies on the frontier compared to the next most cost-effective strategy. We will calculate all cost-effectiveness ratios as cost per life year saved.
2. Health system implementation requirements of point-of-care Xpert HPV testing for the early detection and treatment of cervical pre-cancer lesions. Health system implementation challenges and benefits will be evaluated in terms of:
2.1. Patient-flow and turnaround-time
2.2. Work-flow and staff time
2.3. Training and supervision needs
2.4. Procedures for finance, payment and health information
2.5. Logistics and management
2.6. Shifts in client-provider relationships when moving from current routine screening (based on VIA alone or Pap test) to HPV-based screening.
3. Acceptability of point-of-care Xpert HPV testing for the early detection and treatment of cervical pre-cancer lesions:
3.1. Acceptability of the intervention from client and health provider perspectives will be analysed using quantitative and qualitative methods
3.2. Key findings from each approach will be triangulated in order to allow robust conclusions to be made regarding acceptability.
3.3. We will calculate the proportion of women who consider the intervention ‘acceptable’ or ‘highly acceptable’ using quantitative data collected in study-specific CRFs
3.4. Qualitative data will be collected from study participants, clinic staff, health managers and other key stakeholders in the pre-intervention and intervention phases of the study in focus group discussions (FGDs) and semi-structured interviews (SSIs) that will investigate women’s preferences for service delivery and the wider societal and cultural contexts within which the acceptability of new interventions for cervical cancer are framed and perceived.
4. Laboratory performance of self-collected vaginal specimens compared with clinician-collected cervical specimens for the detection of cervical cancer biomarkers. Laboratory performance characteristics (sensitivity, specificity, positive and negative predictive value) of self-collected compared with clinician-collected specimens for the detection of cervical cancer biomarkers will be calculated as proportions with 95% confidence intervals.

Overall study start date
01/07/2017

Completion date
30/03/2021

Eligibility

Key inclusion criteria

1. Aged 30-59 years
2. Attending a participating Well Woman Clinic
3. Willing to provide self-collected vaginal swabs for baseline Xpert HPV testing
4. Willing to comply with study follow-up procedures
5. Willing to undergo a clinical interview and pelvic examination
6. Willing to provide self-collected and clinician-collected specimens for laboratory investigations
7. Able to complete study informed consent procedures, to understand why the study is being carried out, and the potential risks and benefits associated with study participation;
8. Able to provide reliable contact details to facilitate future community tracing and follow-up

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Female

Target number of participants
4000

Total final enrolment
4285

Key exclusion criteria
1. Currently pregnant or given birth in the last 6 weeks
2. Previous diagnosis of cervical cancer and/or has had a hysterectomy
3. Permanent disability, that prevents or impedes study participation and/or comprehension (such that it is not possible to obtain informed consent to participate)
4. Women having their menstrual period at the time of the clinic visit will be advised to return for screening in 1-2 weeks

Date of first enrolment
06/06/2018

Date of final enrolment
30/12/2020

Locations

Countries of recruitment
Australia

Papua New Guinea

Study participating centre
Papua New Guinea Institute of Medical Research
Homate Street

Goroka
Australia
EHP 441

Sponsor information

Organisation
Kirby Institute UNSW Sydney

Sponsor details
Kirby Institute
Wallace Wurth
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2052

Sponsor type
University/education

Website
https://kirby.unsw.edu.au/

ROR
https://ror.org/03r8z3t63

Funder(s)

Funder type
Not defined

Funder Name
National Health and Medical Research Council

Alternative Name(s)
NHMRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Australia

Results and Publications

Publication and dissemination plan

The investigators are committed to maintaining on-going communication with participating sites and key stakeholders throughout the duration of the study. This will occur through the following mechanisms:
1. Six-monthly newsletters prepared for study participants, local stakeholders and clinical staff at study sites documenting progress with each stage of the trial, emerging issues, upcoming events and new staffing. These newsletters will be disseminated to study sites and key local and national stakeholders including community leaders, national and provincial health departments, and other relevant organisations.
2. Six-monthly summary activity reports for participating trial sites describing enrolment and retention figures, HPV tests conducted and the proportion positive.
3. Six-monthly written updates to key stakeholders at national and provincial level providing an overview of the progress of the study. Presentations will also be provided to participating health authorities and stakeholder organisations as requested.
4. A dedicated study-specific website will be established and used as a platform to disseminate progress updates. We will make these available throughout the course of the study as open access format reports and slide presentations; video updates from the field, including site visits and interviews with in-country policy makers; and interactive webinars (e.g. on study rationale, progress and anticipated impact delivered by senior scientists). The website will maintain an up to date database of research publications in the area of HPV-based cervical screening, and provide links to new findings as they become available in the scientific literature. We will evaluate the success and impact of these electronic resources according to the number of views received per day, number of resources downloaded and participation in webinars.
5. A two-day National Policy Forum on completion of the study to enable senior health care managers, policy makers and development partners to engage with the research team in understanding the implications of our research findings for future public health policy. The forum will be preceded by early consultation with national and provincial policy-makers, to establish locally meaningful benchmarks for feasibility and cost-effectiveness, so that any impact statements presented in the forum can address both international norms and local priorities for sustainability.

Intention to publish date

30/09/2021

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?
Protocol file	version 0.4	30/09/2019	18/08/2021	No	No

Results article	22/07/2022	26/07/2022	Yes	No